DUPLICATE

Med. A.

TRANSACTIONS

OF THE

AMERICAN PEDIATRIC SOCIETY

TWENTY-THIRD SESSION

HELD AT THE LAKE MOHONK MOUNTAIN HOUSE, LAKE MOHONK, N. Y.
MAY 31 TO JUNE 2, 1911

EDITED BY

LINNAEUS EDFORD LA FÉTRA, M.D.

194065
5.2.25.

VOLUME XXIII.

RJ
1
A6
v.23

American Medical Association Press
Five Hundred and Thirty-Five Dearborn Avenue
CHICAGO

CONTENTS

List of Presidents ix

List of Officers for the Year 1911 ix

List of Meeting Places ix

List of Members x

List of Deceased Members xii

Minutes of the Twenty-Third Annual Meeting 1

I. President's Address: The Fundamental Principles of Pediatrics. By Dr. Henry Dwight Chapin, New York 6

II. The Fundamental Requirements of An Infant's Nutrition. By Dr. John Howland 13

III. Protein Metabolism in Infants and Children. By Dr. Herman Schwartz 20

IV. The Rôle of Mineral Salts in the Metabolism of Infants. By Dr. B. Raymond Hoobler 44

V. Studies in the Metabolism of Atrophic Infants. By Dr. Charles A. Fife and Borden S. Veeder 81

VI. Ward Problems. By Dr. Francis Huber 93

VII. (a) Recurrence of Scarlet Fever. (b) Duodenal Ulcer in Early Life. By Dr. J. P. Crozer Griffith 102

VIII. Ward Improvements: Crib Warmer: Management of "Carriers:" Prevention of Epidemics; Children's Service, Presbyterian Hospital. By Dr. W. P. Northrup 108

IX. Hospitals for the Care of Infants and Children and the Methods of Prevention of Infection. By Dr. Henry Koplik 118

X. The Treatment of Sepsis in Scarlatina with Antistreptococcus Serum. By Dr. Matthias Nicoll 136

XI. The Therapeutic Utility of Diphtheria Antitoxin, with Remarks on Anaphylaxis and on the Feasibility of a Scratch Test. By Dr. Augustus Caillé 147

XII. The Treatment of Pertussis with Vaccine. By Dr. Edwin E. Graham 157

XIII. The Radical Removal of the Tonsils and Adenoids. By Dr. Charles G. Kerley 167

XIV. The Occurrence of Infantile Paralysis in the United States and Canada in 1910. By Dr. Robert W. Lovett 175

XV. The Cerebral Forms of Poliomyelitis. By Dr. Henry Koplik 186

XVI. Infantile Paralysis. By Dr. John Lovett Morse 205

XVII. The Control of Epidemic Poliomyelitis. By Dr. Simon Flexner 210

XVIII. The Most Promising Outlook for Improvement in Treatment from the Standpoint of the Pediatrician. By Dr. J. H. Mason Knox.... 217

XIX. Report of Special Committee on Poliomyelitis..... 222

XX. The Polygraph as an Aid in Studying Cardiac Decompensation in Children. By Drs. Godfrey R. Pisek and T. Homer Coffen..... 229

XXI. Diabetes Mellitus in a Seven Months' Old Child. By Drs. P. J. Eaton and E. B. Woods..... 244

XXII. A Note Concerning the Occurrence of Hippuric Acid in the Urine of Normal Breast-Fed Infants. By Drs. Samuel Amberg and J. H. Mason Knox, Jr..... 249

XXIII. A Preparatory Study of the Bacillus Acidophilus in Regard to Its Possible Therapeutic Use. By Drs. Thomas Morgan Rotch and Arthur I. Kendall..... 253

XXIV. The Surgical Management of Acute Abscesses of Lymphatic Glands in Infancy. By Dr. Thomas S. Southworth..... 264

XXV. Which Is Preferable in Colon Irrigations: The Long or the Short Tube? A Comparison Based on Two Hundred Irrigations. By Dr. Henry T. Machell..... 269

XXVI. Drainage Tube in Pleural Cavity. (Removed with Aid of Fluoroscopic Screen.) By Dr. Francis Huber..... 274

XXVII. A Ready Method of Calculating Milk Formulas of Various Percentages and the Caloric Value of the Same. By Dr. L. Emmett Holt..... 278

XXVIII. The Use of Malt Sugar and High Percentages of Casein in Infant Feeding. By Dr. John Lovett Morse..... 285

XXIX. Albumin Milk as Contrasted with Other Milk Mixtures in the Treatment of the Diarrheas of Children. By Dr. Henry Heiman... 300

XXX. Requisite Standards for Raw Materials in the Successful Substitute Feeding of Infants. By Dr. Henry L. Coit..... 306

XXXI. The Acid Control of the Pylorus in Infants. By Drs. D. Murray Cowie and William D. Lyon..... 313

XXXII. Pyloric Stenosis in Older Children, with the Report of a Case of Pyloric Spasm Ending Fatally in a Boy Aged Six and a Half Years. By Dr. Edwin E. Graham..... 324

XXXIII. Muscular Hypertrophy of the Pylorus in Infancy. By Drs. Henry Larned Keith Shaw and Thomas Ordway..... 333

XXXIV. A Discussion of Mikulicz' Disease, with Report of a Case of Lymphatic Leukemia in a Child with Marked Enlargement of the Salivary Glands. By Dr. Wilder Tileston..... 356

XXXV. Clinical and Pathological Study of Amyotonia Congenita. By Drs. J. P. Crozer Griffith and William G. Spiller..... 366

XXXVI. Some Further Observations on the Soy Bean. By Dr. John Ruhräh..... 386

PRESIDENTS

1889. A. Jacobi, M.D.
1890. J. Lewis Smith, M.D.
1891. T. M. Rotch, M.D.
1892. Wm. Osler, M.D.
1893. A. D. Blackader, M.D.
1894. John M. Keating, M.D.
1895. F. Forchheimer, M.D.
1896. Joseph O'Dwyer, M.D.
1897. Samuel S. Adams, M.D.
1898. L. Emmett Holt, M.D.
1899. Wm. P. Northrup, M.D.
1900. Henry Koplik, M.D.
1901. Wm. D. Booker, M.D.
1902. W. S. Christopher, M.D.
1903. J. P. Crozer Griffith, M.D.
1904. Augustus Caillé, M.D.
1905. C. G. Jennings, M.D.
1906. A. Jacobi, M.D.
1907. B. K. Rachford, M.D.
1908. C. G. Kerley, M.D.
1909. Charles P. Putnam, M.D.
1910. David L. Edsall, M.D.
1911. Henry Dwight Chapin, M.D.
1912. Walter Lester Carr, M.D.

OFFICERS, 1911

President ..... Henry Dwight Chapin, M.D.
Vice-President ..... J. H. M. Knox, M.D.
Secretary ..... Samuel S. Adams, M.D.
Treasurer ..... Chas. Hunter Dunn, M.D.
Recorder and Editor ..... L. E. La Fétra, M.D.

COUNCIL

John Lovett Morse, M.D., *Chairman*

S. McC. Hamill, M.D.
Geo. N. Acker, M.D.
R. G. Freeman, M.D.
Alfred Hand, Jr., M.D.
L. E. LaFétra, M.D.
Isaac A. Abt., M.D.

MEETING PLACES

1888. Washington, D. C. (Organization), September 18.
1889. Washington and Baltimore, September 20 and 21.
1890. New York, June 3 and 4.
1891. Washington, September 22 and 25.
1892. Boston, May 2, 3 and 4.
1893. West Point, N. Y., May 24, 25 and 26.
1894. Washington, May 29 and June 1.
1895. Virginia Hot Springs, May 27, 28 and 29.
1896. Montreal, May 25, 26 and 27.
1897. Washington, May 4, 5 and 6.
1898. Cincinnati, June 1, 2 and 3.
1899. Deer Park, June 27, 28 and 29.
1900. Washington, May 1, 2 and 3.
1901. Niagara Falls, May 27, 28 and 29.
1902. Boston, May 26, 27 and 28.
1903. Washington, May 12, 13 and 14.
1904. Detroit, May 30, 31 and June 1.
1905. Lake George, N. Y., June 19, 20 and 21.
1906. Atlantic City, N. J., May 30, 31 and June 1.
1907. Washington, May 7, 8 and 9.

1908. Delaware Water Gap, May 25, 26 and 27.
1909. Lenox, Mass., May 27 and 28.
1910. Washington, May 3, 4 and 5.
1911. Lake Mohonk, N. Y., May 31 and June 1 and 2.
1912. Hot Springs, Va., May 29, 30 and 31.

OFFICERS, 1912

President ..... Walter Lester Carr, M.D.
Vice-President ..... P. J. Eaton, M.D.
Secretary ..... Samuel S. Adams, M.D.
Treasurer ..... Chas. Hunter Dunn, M.D.
Recorder and Editor ..... L. E. La Fétra, M.D.

COUNCIL

S. McC. Hamill, M.D., *Chairman.*

Geo. N. Acker, M.D. — L. E. LaFétra, M.D.
R. G. Freeman, M.D. — Isaac A. Abt., M.D.
Alfred Hand, Jr., M.D. — John Howland, M.D.

MEMBERS

Abt, Isaac A., M.D. ..... 4326 Vincennes Avenue, Chicago
Acker, George N., M.D. ..... 913 Sixteenth Street, Washington
Adams, Samuel S., M.D. ..... 1 Dupont Circle, Washington
Baines, Allen M., M.D. ..... 228 Bloor Street, Toronto
Blackader, A. D., M.D. ..... 236 Mountain Street, Montreal
Bovaird, David, Jr., M.D. ..... 137 East Sixtieth Street, New York
Bowditch, Henry I., M.D. ..... 416 Marlborough Street, Boston
Butterworth, William W., M.D. ..... Tulane Univ., New Orleans, La.
Caillé, Augustus, M.D. ..... 753 Madison Avenue, New York
Carpenter, Howard C., M.D. ..... 1805 Spruce Street, Philadelphia
Carr, Walter Lester, M.D. ..... 68 West Fifty-first Street, New York
Chapin, Henry Dwight, M.D. ..... 51 West Fifty-first Street, New York
Churchill, F. S., M.D. ..... 1259 North State Street, Chicago
Coit, Henry L., M.D. ..... 277 Mt. Prospect Avenue, Newark, N. J.
Cotton, A. C., M.D. ..... 1485 Jackson Boulevard, Chicago
Cowie, D. M., M.D. ..... Lawrence Building, Ann Arbor, Mich.
Crandall, Floyd M., M.D. ..... 113 West Ninety-fifth Street, New York
Dorning, John, M.D. ..... 124 West Eighty-first Street, New York
Dunn, Charles Hunter, M.D. ..... 220 Marlborough Street, Boston
Eaton, Percival J., M.D. ..... 131 N. Highland Avenue, E. E., Pittsburgh
Edsall, David L., M.D. ..... 1432 Pine Street, Philadelphia
Fife, Charles A., M.D. ..... 1927 Chestnut Street, Philadelphia
Forchheimer, F., M.D. ..... Fourth and Sycamore Streets, Cincinnati
Freeman, Rowland G., M.D. ..... 211 West Fifty-seventh Street, New York
Gittings, J. C., M.D. ..... 3492 Chestnut Street, Philadelphia
Graham, E. E., M.D. ..... 1713 Spruce Street, Philadelphia
Griffith, J. P. Crozer, M.D. ..... 1810 Spruce Street, Philadelphia
Hamill, S. McC., M.D. ..... 1822 Spruce Street, Philadelphia
Hand, Alfred, Jr., M.D. ..... 1724 Pine Street, Philadelphia
Haynes, Royal S., M.D. ..... 267 West Seventy-ninth Street, New York
Heiman, Henry, M.D. ..... 30 West Eighty-eighth Street, New York
Herrman, Charles, M.D. ..... 250 West Eighty-eighth Street, New York
Holt, L. Emmett, M.D. ..... 14 West Fifty-fifth Street, New York

HOWLAND, JOHN, M.D. ..... 1806 Locust Street, St. Louis
HUBER, F., M.D. ..... 209 East Seventeenth Street, New York
JACOBI, A., M.D. ..... 19 East Forty-seventh Street, New York
JENNINGS, CHARLES G., M.D. ..... 457 Jefferson Avenue, Detroit
KERLEY, CHARLES G., M.D. ..... 132 West Eighty-first Street, New York
KNOX, J. H. MASON, M.D. ..... 804 Cathedral Street, Baltimore
KOPLIK, HENRY, M.D. ..... 30 East Sixty-second Street, New York
LADD, MAYNARD, M.D. ..... 270 Clarendon Street, Boston
LA FÉTRA, LINNÆUS E., M.D. ..... 113 East Sixty-first Street, New York
LUCAS, WILLIAM PALMER, M.D. ..... 261 Beacon Street, Boston
MACHELL, H. T., M.D. ..... 95 Bellevue Avenue, Toronto
MEARA, FRANK S., M.D. ..... 400 West End Avenue, New York
MILLER, D. J. MILTON, M.D. ..... 127 S. Illinois Avenue, Atlantic City, N. J.
MORSE, J. LOVETT, M.D. ..... 70 Bay State Road, Boston
NICOLL, MATTHIAS, M.D. ..... 124 East Sixtieth Street, New York
NORTHRUP, WILLIAM P., M.D. ..... 57 East Seventy-ninth Street, New York
PISEK, GODFREY R., M.D. ..... 36 East Sixty-second Street, New York
PUTNAM, CHARLES P., M.D. ..... 63 Marlborough Street, Boston
RACHFORD, B. K., M.D. ..... 323 Broadway, Cincinnati
ROTCH, THOMAS MORGAN, M.D. ..... 197 Commonwealth Avenue, Boston
RUHRÄH, JOHN, M.D. ..... 839 North Eutaw Street, Baltimore
SAUNDERS, E. W., M.D. ..... 3003 Lafayette Avenue, St. Louis, Mo.
SHAW, HENRY L. K., M.D. ..... 361 State Street, Albany
SNOW, IRVING M., M.D. ..... 476 Franklin Street, Buffalo
SOUTHWORTH, THOMAS S., M.D. ..... 807 Madison Avenue, New York
STARR, LOUIS, M.D. ..... 1818 Rittenhouse Square, Philadelphia
TALBOT, FRITZ B., M.D. ..... 311 Beacon Street, Boston
TILESTON, WILDER, M.D. ..... 308 Crown Street, New Haven
TOWNSEND, CHARLES W., M.D. ..... 76 Marlborough Street, Boston
WENTWORTH, A. H., M.D. ..... 352 Marlborough Street, Boston
WESTCOTT, THOMPSON S., M.D. ..... 1720 Pine Street, Philadelphia
WILLIAMS, HAROLD, M.D. ..... 528 Beacon Street, Boston
WINTERS, J. E., M.D. ..... 25 West Thirty-seventh Street, New York

HONORARY MEMBERS

DR. JOHN THOMPSON ..... Edinburgh, Scotland
DR. GEORGE F. STILL ..... London, England
DR. O. HEUBNER ..... Berlin, Germany
DR. WILLIAM OSLER ..... Oxford, England
DR. A. BAGINSKY ..... Berlin, Germany
DR. V. HUTINEL ..... Paris, France
DR. CHARLES RAUCHFUSS ..... St. Petersburg, Russia

Deceased

John A. Jeffries, M.D.
Born, September 2, 1859.
Died, March 26, 1892.

Thomas F. Sherman, M.D.
Born, March 17, 1856.
Died, September 26, 1893.

John M. Keating, M.D.
Born, April 20, 1852,
Died, November 17, 1893.

Charles Warrington Earle, M.D.
Born, 1845,
Died, November 19, 1893.

J. Lewis Smith, M.D.
Born, October 15, 1827,
Died, June 9, 1897.

Joseph O'Dwyer, M.D.
Born, October 12, 1841,
Died, January 7, 1898.

John Henry Fruitnight, M.D.
Born, November 9, 1851.
Died, December 18, 1900.

Frederick A. Packard, M.D.
Born, November 17, 1862.
Died, November 1, 1902.

Walter S. Christopher, M.D.
Born, 1859.
Died, March 2, 1905.

Leroy Milton Yale, M.D.
Born, February 12, 1841,
Died, September 12, 1906.

James Park West, M.D.
Born, June 27, 1858,
Died, June 25, 1908.

MINUTES OF THE TWENTY-THIRD ANNUAL MEETING OF THE AMERICAN PEDIATRIC SOCIETY

Held at the Lake Mohonk Mountain House, Mohonk Lake, N. Y., May 31 to June 2, 1911

The meeting was called to order by the President, Dr. Henry D. Chapin of New York. The following members were present: Drs. George N. Acker, Washington; Samuel S. Adams, Washington; Allen Baines, Toronto; A. D. Blackader, Montreal; Augustus Caillé, New York; Walter Lester Carr, New York; F. S. Churchill, Chicago; Henry L. Coit, Newark; A. C. Cotton, Chicago; D. M. Cowie, Michigan; Floyd M. Crandall, New York; Charles Hunter Dunn, Boston; Percival J. Eaton, Pittsburgh; Charles A. Fife, Philadelphia; Rowland G. Freeman, New York; J. C. Gittings, Philadelphia; E. E. Graham, Philadelphia; J. P. Crozer Griffith, Philadelphia; S. McC. Hamill, Philadelphia; Royal S. Haynes, New York; Henry M. Heiman, New York; Charles Hermann, New York; L. Emmett Holt, New York; John M. Howland, New York; A. Jacobi, New York; Charles G. Jennings, Detroit; Charles G. Kerley, New York; J. H. M. Knox, Baltimore; Henry Koplik, New York; L. E. LaFétra, New York; H. T. Machell, Toronto; Frank S. Meara, New York; J. Lovett Morse, Boston; Matthias Nicoll, New York; William P. Northrup, New York; Godfrey R. Pisek, New York; Thomas Morgan Rotch, Boston; John Ruhräh, Baltimore; Henry L. Shaw, Albany; Irving M. Snow, Buffalo; Thomas S. Southworth, New York; Wilder Tileston, New Haven; Thomas S. Westcott, Philadelphia; J. E. Winters, New York.

There were present as guests: Drs. S. V. Haas, New York; Harold J. Morgan, Toledo, Ohio; Herman Schwartz, New York; Borden S. Veeder, Philadelphia; O. D. Kingsley, Mohonk Lake; Van der Bogert, Schenectady; F. M. Fry, Montreal; Langley Porter, San Francisco; and Dr. Cushing of Montana.

The minutes of the twenty-second annual meeting were adopted as published in the *Archives of Pediatrics.*

The following papers were read:

1. President's Address: Dr. Henry D. Chapin: "The Fundamental Principles of Pediatrics."

SYMPOSIUM ON METABOLISM

2. Dr. John Howland: "The Fundamental Requirements of the Infant's Nutrition."

3. Drs. Frank S. Meara and Herman Schwartz: "The Metabolism of Proteins."

4. Drs. Frank S. Meara and B. Raymond Hoobler: "The Metabolism of Salts."

5. Dr. Charles A. Fife: "Studies in the Metabolism of Atrophic Infants."

6. Dr. Charles Hermann: "A Study of One Hundred Infants from Birth to the End of the First Year."

7. Dr. J. P. Crozer Griffith: (*a*) "Recurrence of Scarlet Fever." (*b*) "Duodenal Ulcer in Early Life."

8. Dr. William P. Northrup: "Ward Improvements; Crib Warmer; Management of Carriers; Prevention of Epidemics; Children's Service, Presbyterian Hospital."

9. Dr. Henry Koplik: "Hospitals for the Care of Infants and Children and the Methods of Prevention of Infection."

These papers were discussed by Drs. Northrup, Holt, Kerley, Jacobi, Rotch, Machell, Morse, Eaton, Churchill, Caillé, Pisek, Blackader, Southworth, Adams, LaFétra, Freeman and Koplik.

---

10. Dr. Matthias Nicoll: "Treatment of Sepsis in Scarlatina with Antistreptococcus Serum."

11. Dr. Caillé: "The Therapeutic Utility of Diphtheria Antitoxin. With Remarks on Anaphylaxis and the Feasibility of a Scratch Test."

This paper was discussed by Drs. Graham, Pisek, Knox, Snow, Nicoll, Kerley, Ruhräh, Eaton and Caillé.

12. Dr. Ruhräh: "An Exhibition of the Bass and Watkins Microscopic Agglutination Test for Typhoid Fever."

13. Drs. J. C. Gittings and George Feterolf: "Anatomical Demonstration of Hardened Bodies of Infants and Children, with Special Reference to Physical Diagnosis."

14. Dr. Henry L. K. Shaw and Dr. Thomas Ordway: "Muscular Hypertrophic Pyloric Stenosis in Infants." (Lantern Slide Demonstration.)

15. Dr. Edwin E. Graham: "The Value of Pertussis Vaccine in the Treatment of Whooping Cough."

16. Dr. Charles Gilmore Kerley: "The Radical Removal of Tonsils and Adenoids."

This paper was discussed by Drs. Rotch, LaFétra, Koplik, Freeman, Haynes, Knox, Chapin, Jacobi and Kerley.

17. Drs. Godfrey R. Pisek and T. Homer Coffen: "The Polygraph as an Aid in Studying Cardiac Decompensation in Children."

This paper was discussed by Drs. LaFétra, Jacobi and Pisek.

18. Drs. Thomas Morgan Rotch and Arthur I. Kendall: "Preparatory Study of the Bacillus Acidophilus in Regard to Its Possible Therapeutic Use."

This paper was discussed by Drs. Morse, Jacobi, Knox, Dunn and Rotch.

19. Dr. J. P. Eaton: "Diabetes Mellitus in a Seven Months Old Child."

This paper was discussed by Drs. Jacobi, Eaton and Kerley.

20. Drs. J. H. Mason Knox and S. Amberg: "A Note on the Absence of Hippuric Acid in the Urine of the Breast-Fed Infant."

SYMPOSIUM ON POLIOMYELITIS

21. Dr. Robert W. Lovett: "The Occurrence of Infantile Paralysis in the United States and Canada in 1910."

22. Dr. Henry Koplik: "The Cerebral Forms of Poliomyelitis."

23. Dr. John Lovett Morse: "Infantile Paralysis."

24. Dr. Simon Flexner: "The Control of Epidemic Poliomyelitis."

25. Dr. Knox: "The Most Promising Outlook for Improvement in Treatment from the Standpoint of the Pediatrician."

26. Dr. Snow: "Report of the Committee of the American Pediatric Society and the American Orthopedic Association."

These papers were discussed by Drs. Adams, Westcott, Chapin, Jacobi, Cotton, Blackader, Churchill, Crandall, Morse, Acker, Machell, Lovett, Flexner, Koplik and Knox.

---

27. Dr. Rowland G. Freeman: "The Preservation of Health in School Children."

This paper was discussed by Drs. Graham, Blackader, Hermann, Morse, Kerley, Adams, Jacobi, Chapin and Freeman.

28. Dr. Thomas S. Southworth: "The Surgical Management of Acute Suppuration of the Lymph Glands in Infancy."

29. Dr. Henry T. Machell: "Which is Preferable in Colon Irrigations, the Long or the Short Tube? A Comparison Based on Two Hundred Irrigations."

This paper was discussed by Drs. Jennings, Jacobi, Chapin and Machell.

30. Dr. Holt: "A New Method of Calculating Milk Percentages."

This paper was discussed by Drs. Blackader, Holt, Churchill, Ruhräh, Freeman, Chapin, Koplik, Knox, Morse, Cowie, Griffith and Kerley.

31. Dr. John Lovett Morse: "The Use of Malt Sugar and of High Percentages of Casein in Infant Feeding."

32. Dr. Henry Heiman: "Albumin Milk as Contrasted with Other Milk Mixtures in the Treatment of the Diarrheas of Children."

These papers were discussed by Drs. Koplik, Jacobi, Rotch, Freeman and Morse.

33. Dr. Henry L. Coit: "Requisite Standards for Raw Materials in the Successful Substitute Feeding of Infants."

34. Drs. D. Murray Cowie and William D. Lyon: "The Acid Control of the Pylorus in Infants."

35. Dr. Edwin E. Graham: "Pyloric Stenosis in Older Children, with the Report of a Case of Pyloric Spasm Ending Fatally in a Boy Aged Six and a Half Years."

36. Dr. Wilder Tileston: "Mikulicz' Disease."

37. Drs. J. P. Crozer Griffith and William G. Spiller: "Clinical and Pathological Study of Amyotonia Congenita."

The following papers were read by title:

"Ward Problems," by Dr. Francis Huber, New York.

"Some Further Observations on the Soy Bean," by Dr. John Ruhräh, Baltimore.

"A Study of Adherent Pericardium by the Radiograph and Pulse Tracings," by Dr. David Bovaird, New York.

EXECUTIVE SESSION, MAY 31, 8 P. M.

The report of the Council was read by Dr. J. Lovett Morse and its recommendations were adopted as follows:

As officers for the ensuing year:

President, Dr. W. L. Carr, New York; Vice-President, Dr. P. J. Eaton, Pittsburgh; Secretary, Dr. Samuel S. Adams, Washington; Recorder and Editor, Dr. L. E. LaFétra, New York; Member of Council, Dr. J. Howland, New York; Member of Executive Committee of Congress of American Physicians and Surgeons: Delegate, Dr. Jacobi, New York; Alternate, Dr. Griffith, Philadelphia.

The excuse for absence of Dr. Putnam was read and accepted.

The following were recommended for membership:

Drs. William W. Butterworth, New Orleans; Howard C. Carpenter, Philadelphia; Fritz B. Talbot, Boston; William Palmer Lucas, Boston; and Henry Ingersol Bowditch, Boston.

As the place and time of next meeting, Hot Springs, Va., May 29, 30 and 31, 1912.

The report of Treasurer was audited by Dr. LaFétra and found correct.

An annual assessment of $15 was levied.

The proposition of Treat & Co. was not accepted.

A committee of two was instructed to arrange for publication of Transactions to be appointed by chair.

The resignations of Drs. Buckingham and Martin were accepted with regrets.

It was recommended that a sufficient sum be appropriated by Society to meet expenses of Joint Committee.

The following were proposed for membership: Dr. McLanahan, Omaha, Neb., by Drs. Griffith and Morse; Dr. Eli Long, New York City, by Drs. Nicoll and Pisek; Dr. A. C. Eastman, Springfield, Mass., by Drs. Kerley and Dunn; Dr. William Shannon, by Drs. Kerley and Winters; Dr. O. M. Schloss, by Drs. Southworth and Pisek; Dr. Borden S. Veeder, Philadelphia, by Drs. Howland and Fife; Dr. B. Raymond Hoobler, by Drs. Northrup and Haynes; Dr. S. V. Haas, New York, by Drs. Kerley and Holt; Dr. Langley Porter, San Francisco, by Drs. Kerley and Holt; Dr. Herman Schwartz, New York, by Drs. Kerley, Koplik and Holt.

On motion of the Secretary a vote of thanks was extended to the President of the Society and to the management of the hotel. Motion seconded and carried.

The Society adjourned to meet at Hot Springs, Va., May 29 and 30, 1912.

SAMUEL S. ADAMS, Secretary.
LINNÆUS E. LAFÉTRA, Recorder.

THE FUNDAMENTAL PRINCIPLES OF PEDIATRICS

HENRY DWIGHT CHAPIN, M.D.
NEW YORK

PRESIDENT'S ADDRESS

Pediatrics, at present, may be divided into two parts: first, that relating to the treatment of disease and perversion of function; second, that concerned with the production of well-developed physique in children. More attention is usually paid to the first than to the second of these branches.

If its scope were broadened, pediatrics might be defined as that branch of science which concerns itself with the animal aspect of the production of human beings. This science could then be divided into two parts: first, that devoted to the production of the highest development of the human being as an animal; second, that concerned with the management of the growing human animal when malformed, or with perverted functions, or subjected to mechanical injury, or attacked by parasitic microorganisms, or poisoned. It is evident then, that the pediatrist should be versed in general biology, bacteriology, protozoology, chemistry and physics.

While the public is not yet fully educated to the advantages of consulting a pediatrist before children are sick, it would be to the advantage of children, of parents, and of the community at large if every child during its most active period of growth were supervised by a well-equipped pediatrist, meaning by this, one who has had a broad training in general science as well as in a special department of medicine. If a physician undertakes to look after the development of a child, he should thoroughly understand the broad principles of human development and of animal life in general; it is not enough simply to be able to follow the ideas of some prominent teacher or authority.

It would prove an advantage to all physicians if the fundamental principles of the management of infants could be firmly established and thus taken out of the field of discussion. In order to attain this result, it is essential that the teachings concerning the chemistry of feeding be in accord with the general science of chemistry, that the problems of infancy falling in the province of physics be recognized as such, and that the teachings concerning animal life and development be true to those principles which have been found to apply to life in all its forms.

While medical men stand well in the forefront when it comes to the relations of human beings and animals to bacteria and protozoa, it must be confessed that they often lag behind in respect to the general care, nutrition and development of the human being in relation to his environment. The physician may broaden out to advantage at the points where science at large touches these problems.

The life-cycle of human beings, like that of all forms of animal life, may be sharply divided into two periods: first, that in which all of the food is derived from the mother's body in specialized forms; second, that in which none of the food is obtained from the mother's body but a wide variety of forms is taken. It is during the period in which the mother secretes the specialized forms of food that the tissues are produced and become differentiated into organs. When the organs of nutrition are developed, such forms of food are no longer needed and the infant has become a living machine that is able from food to build the future adult. This living machine is operated on much the same principle as a mechanical engine. It takes in fats, sugars and starches, and by combining them with air procured through the lungs, obtains a supply of energy. This energy, when expended, appears in the form of heat which must be removed as fast as it is liberated, and it is accordingly found that all animals are provided with two cooling systems. For ordinary conditions radiation of heat into the surrounding air is sufficient, but when the temperature of the air is nearly as high as that of the body, or higher, radiation fails to cool sufficiently, and heat is removed by being changed into latent heat through the evaporation of perspiration.

An infant taking 36 ounces of breast milk daily receives food yielding about 792 calories, or enough heat to raise the temperature of a 14-pound baby 113 C. In other words, this food will liberate enough heat to raise the temperature of the infant above the boiling-point of water. It may easily be appreciated, then, how important is the proper working of the infant's cooling system; yet how few realize that infants and all animals have cooling systems, and that the life habits of many animals are largely controlled by them! Some animals of enormous strength, such as the lion and cat tribe, are incapable of prolonged effort because they cannot get rid of the heat liberated as fast as it is produced.

A large part of the sickness among infants in hot weather may be due to ineffective cooling of the living animal motor. Imagine an infant on a hot day lying in a crib surrounded by curtains. Air movement is stopped, and the atmosphere around the infant becomes so saturated with

water vapor from the evaporated perspiration that no more can evaporate, with the result that the infant's cooling system breaks down and vomiting and diarrhea may ensue. Boiling water, and vapor from it, have the same temperature, 212 F., yet the vapor has absorbed almost 1,000 degrees of heat and rendered it latent or insensible. As long as the air is not saturated with vapor, or is nearly saturated, but in motion, this change from sensible to insensible heat takes place and it is perfectly feasible to be cool and comfortable in air whose temperature is above 100 F., provided this air is dry or in motion and thus capable of vaporizing perspiration. In fact, one can be kept quite cool by a current of hot dry air if a wet cloth is kept next to the skin.

When an infant has been subjected to conditions such as render it unable to liberate its heat properly, the treatment that has proved most successful is to stop all food temporarily, thereby reducing heat production; to give the infant baths to remove heat; to keep it quiet to prevent the expenditure of energy which liberates heat; and to send it to the country where the air is cool or dry or in motion; then, unless there is very acute poisoning, recovery usually takes place.

No doubt bacteria play a large part in the summer sickness of infants, but as they are present in food at all seasons, it is evident that the heat gives them an advantage over the infant which they do not possess in cooler weather, or when conditions are favorable for the infant to rid itself of the heat. Restoring the infant to normal action causes the bacteria to lose their effect.

In hot weather food cannot be needed for its caloric or heating effect; it is required rather for its energy content, and the teaching should be in accordance with this fact. Feeding for energy is, to a large extent, a branch of physics; in the management of summer cases a knowledge of the principles of physics would thus often be of greater value than acquaintance with many of the drugs so often employed. The protein and mineral matter are for building materials and repair, and chemical composition is here the controlling factor, as far as potential value is concerned. It is, however, entirely out of place to value protein by its energy or caloric contents. What would be thought of an architect who determined the suitability of timber for a building by the amount of heat it would produce if burned? The feeding of energy and of building materials must be done with a distinct idea of the purposes they are to serve.

The emphasis on the necessity of plenty of fresh air should not be looked on as a hobby. The animal motor operates by a combination of

oxygen in the air and the fats and carbohydrates of the food, and one is useless without the other. Insufficient air means incomplete combustion, and the products of incomplete combustion clog up the animal motor. Air is thus as essential as food.

In managing the nutrition of the infant much can be learned from general biology. In all forms of animal life the mother supplies specialized forms of food to the young until their digestive organs are developed, and no method of feeding that ignores this fact can be of the highest value. Many years ago I called attention to the fact that the protein of all milks has a developmental as well as a nutritive function. An artificial food for infants should contain the building elements and energy foods in about the same quantities as those in mother's milk if the best development is to result. Attention should likewise be paid to see that the food behaves in the stomach like mother's milk, but it will not do to compare foods by their chemical analyses alone, as it has long been known that two foods of the same chemical composition might not be interchangeable in nutritive value, and there are factors involved in feeding that chemical analysis cannot explain. The reason for this may be found in some of the later work in chemistry, as exemplified in the following illustrations: It is a curious fact that two clays having the same chemical composition may have entirely different physical properties, and that clay near the mouth of a river will have different properties from the same substance further up the stream, the two clays being derived from the same parent rock and having similar compositions. Acheson reasoned that this difference might be due to the fact that the clay down stream had come into contact with washings from organic matter, and by adding vegetable infusions to the upstream clay he was able to increase its plasticity and make it act like the clay down stream. Here is a practical illustration of what profound changes the most insignificant additions to a substance may produce. Bodies that are insoluble in water may be rendered soluble if certain foreign substances are present in the most minute quantities. Duncan gives the following illustration:

> The mere presence of a trace of a foreign body may make an insoluble body soluble. The following puzzling fact is known to but few: chromic chlorid is a curious substance that exists in two forms, soluble and insoluble. The insoluble violet crystals may be left under water for days unaffected . . . but drop into the test-tube a trace of chromous chlorid, even 0.000025 of a gram, and the violet crystals hasten to bury themselves in the water; the temperature rises and the indigo-blue liquid results. This is an example of what is called physical catalysis, for the chemical properties of the chromic chlorid are the same after as before; it has simply passed into solution. Turning now to chemical catalysis, we are

confused by the number of examples, for, owing to the recent ferment of investigation, it would take a dictionary to chronicle them.

Remarkable results have been obtained in industrial chemistry by the use of such catalysts. Substances which have been obtained indirectly by the aid of plants can now be made artificially. Heretofore, when the necessary ingredients to form desired substances were brought together, they would not combine. There was something in the plants, however, that would cause such combinations to take place. Indigo has been obtained from the indigo plant, but it was found that the mere presence of a trace of copper or mercury would make the ingredients combine in the laboratory, and now it is made artificially. Platinum black is used to cause the ingredients of formaldehyd to combine, and other substances will cause metallic gold, silver, platinum and graphite to go into aqueous solution called colloidal solution.

How many factors in feeding may be influenced by such apparent trifles remain to be discovered, but that numbers of the vital processes are thus controlled is beyond doubt. Hunt makes the following statement:

> Diet has a marked effect on the resistance of animals to certain poisons; the resistance of some animals may be increased forty-fold by changes in diet. Certain diets, notably dextrose, oatmeal, liver, and kidney, greatly increase the resistance of mice to acetonitrile; their effect is similar in this respect to the administration of thyroid; the effect of an oatmeal diet in increasing the resistance of certain animals to acetonitrile is probably due, in part, to a specific effect of the diet on the thyroid gland; this is an illustration of how an internal secretion may be modified in a definite manner by diet. . . . The experiments show that foods such as enter largely into the daily diet of man have most pronounced effects on the resistance of animals to several poisons; they produce changes in metabolism which are not readily detectable by methods ordinarily used in metabolism studies. The ease and rapidity with which certain changes in function are caused by diet are in striking contrast with the essentially negative results obtained by the chemical analyses of animals fed on different diets.

According to Alexander:

> Bald chemical analyses cannot express the digestibility and availability of a food any more than it can express or explain the action of the digestive juices, or, in fact, any other physiologic process. In all these processes can be traced the influence of the colloidal substances, present in the body, whose effects are quite out of proportion to their small mass. As soon as we approach the chemistry of the living organism, we are confronted with problems of colloid chemistry, and there is no doubt but that a correct understanding and application of its principles will throw much light on many other obscure problems in biology, physiology and medicine.

These foreign bodies, whose mere presence causes such profound changes, are called catalysts, and a peculiar property which they possess is that at times they lose their efficiency. When this occurs they are said

to be poisoned. After a time they may recover their power to produce the changes they formerly caused.

The question as to what this has to do with the practical management of infants may here be raised. McCullom conducted some experiments to see how simple in form the food elements could remain and still be combined in the animal body, it long having been believed that animals could not live for any length of time and develop on the pure food elements. Pure fat, sugar, starch, ash-free protein and the ash of milk were used, filter-paper being employed to give bulk. For a time there was gain, then a standstill and finally a loss. By adding successively such flavoring agents as cinnamon, celery, vanilla, caramelized sugar, distillate from strong cheese and salt, it was found that the loss could be prevented. Leaving the fat out of the food temporarily or changing its form, or altering the sugar content of the food was found to improve the utilization of the food. "In one instance toward the end of the experiment, bacon fat, freshly rendered and filtered through paper, induced hearty consumption when every other means failed." His conclusions were as follows:

> Without palatability the ration may possess all the necessary food ingredients and yet fail to nourish an animal properly. The failure of previous efforts to maintain animals on a mixture of relatively pure, proximate constituents of our foodstuffs was due to lack of palatability of such mixtures. When sufficient care is given to changing the character and flavor of the food supplied in such simple mixtures, it is possible to induce an appreciable amount of growth.

Here is an illustration of the action of catalysts in practical feeding. One worked well until it became poisoned or lost its efficiency. A change in the form or flavor of the food brought another catalyst into action, and it in turn lost its efficacy. The beneficial effect of variety of diet has long been known, but the scientific basis on which it rested has not been suspected hitherto. We often get the same good effect by changing the flavor of the infant's food or by altering the form of the food elements, especially the carbohydrates.

Such facts as these could never have been explained by practical infant-feeding, or rather, the principles could not have been evolved; and this shows the advantage of being familiar with general science and applying principles worked out elsewhere to the management of infants.

That a profound change in the function of the human digestive organs may be brought about by changing the character of the food has been shown by Yakawa, who fed young men who had been vegetarians all their lives a diet composed largely of beef, milk, eggs and rice. The fats, and particularly the protein, were not well assimilated. There was loss of

appetite, lassitude and constipation. Such a result is at variance with the belief held generally that animal protein is better digested than vegetable protein. But this case is an illustration of the biologic principle that all living things tend to adapt themselves to their food and environment. Those who have been trained to digest animal protein develop digestive organs well fitted for this purpose and digest it better than they do vegetable protein, and vice versa.

It has been said that one principle is worth many facts, for it covers them all. If the few main principles in pediatrics could be grasped, a large number of facts might be forgotten to advantage. Pediatrics cannot take the position it deserves until those who practice it recognize that their work is to help infants adapt themselves to their food and environment, and this calls for at least an elementary knowledge of general biology, bacteriology, protozoology, chemistry and physics. We must broaden our scientific outlook.

Medicine has always advanced more rapidly as an art than as a science, partly because it has not been sufficiently rooted in the principles and methods of general science. The extreme growth and differentiation of specialism has here acted both as cause and effect. Ingenious and successful technic, rather than the more laborious and widely applicable study of underlying principles, has often satisfied. The specialties themselves have been accepted without much appreciation of their relative values. Those of fundamental importance are grouped with others having only local forms that minister to comfort and utility, but not often directly to life itself. It is thus right to make a distinction between a major and a minor specialty. Of the former, pediatrics should take the highest place, as it deals with the first and formative period of life, and consequently renders the most lasting service to the race. It is time that a new account of stock be taken of the various branches of medicine and that they be lined up with a truer perspective as to relative importance. Thus will the dignity and importance of pediatrics be made clear to the profession and the public. It offers to-day the most promising field for advanced work in scientific and experimental medicine. Fully to occupy this field, its followers must apply the general and broad methods of science at large to the solution of its problems.

One of the deepest sayings of Sir Francis Bacon was: "The end of philosophy is the intuition of unity." Let us apply this broad truth to science. The end and object of all science is the recognition of unity.

THE FUNDAMENTAL REQUIREMENTS OF AN INFANT'S NUTRITION

JOHN HOWLAND, M.D.
ST. LOUIS

The requirements for an adult's nutrition under the most varying circumstances are definitely known. The amount of food that is necessary to keep him in a state of equilibrium when at rest, when exercising moderately and when undergoing the most violent exertions, has been determined with scientific accuracy. These determinations may be repeated as often as wished, and, provided they are properly made, will give uniform results. They are laborious and time-consuming, but yield trustworthy data because, with the assent and the cooperation of the adult subject, the conditions can be absolutely controlled.

It is not so with children or infants. There is no reason to believe that in them the laws of nutrition differ in any marked way from those of the adult, but the control of conditions so as to make our results trustworthy is extremely difficult, and we are able to obtain, at best, only a part of the information that we wish, accurate though this be. I shall speak of this more fully later, because it is the one, and apparently the only, insurmountable obstacle in the way of the most scientific and satisfactory accuracy in determining the food requirements of the infant.

There are certain fundamental facts that must be considered in dealing with this subject. The warm blooded animal requires energy for the life processes of the organism, the heart-beat and circulation, the respiration and the activity of the various organs and glands, and the heat produced by these processes, with the assistance of the physical vasomotor control, maintains the cells at their normal tropical temperature, in which they functionate to the best advantage. Energy is also required in addition for the animal's endless muscular activities. The energy that the body expends is all given off and may be measured as heat — all except that energy contained in substances in the urine and feces that have failed of complete combustion and which for the present may be disregarded. It is therefore quite logical to speak of the energy expended in terms of heat-units and of the food that is ingested to furnish this energy and which is readily converted into it, in the same terms.

If the output is known, the human body may be retained in a state of equilibrium by furnishing an amount of energy in the form of food equal to this, and, as I have said, the output is, especially in adults, capable of being measured. It is obviously impossible to do this for each patient that must be fed, but Rubner's work makes this no longer necessary. Pettenkofer and Voit measured the output of different men under the same conditions, but were unable to decide what it was that determined the varying amount of energy loss. It was Rubner's great service to point out that the heat production and dissipation, or, in other words, the amount of energy lost, are, under similar circumstances, proportional to the surface area of the body. This law enjoys the widest applicability. The lion and the mouse, the infant, the grown man and the giant give off the same amount of heat per square meter of body surface, provided the conditions are the same. The importance of the skin surface is thus apparent.

An accurate method for the determination of the body's surface area is, therefore, necessary. The formula usually employed is

$$\sqrt[3]{\text{Wt. in gm.}}^{2}$$

multiplied by a constant, 12.3 or 11.9. For the average well-nourished child or adult, this formula gives excellent results. It is not, I believe, from the results of some of our experiments, accurate for poorly nourished or emaciated beings, and a formula which will give information as to the surface area of these is desirable and capable of being constructed.

We are further indebted to Rubner for determining by a series of thorough and painstaking experiments the utilization of the various foodstuffs and the amount of energy that each is capable of furnishing to the body under normal conditions of digestion, assimilation and excretion. Fat furnishes to the body 9.3 calories of energy per gram ingested, sugar 4.1 and protein 4.1, without reference to the products of incomplete combustion that are eliminated in the urine and feces. The saving of labor as a result of these determinations has been immeasurable, and it is because of these determinations that we may disregard the elimination of the products of incomplete combustion in the urine and feces.

In order to determine the food requirements of an infant, we begin with the assumption that the energy required to keep him in a state of equilibrium is equal to his output. If then, we measure accurately his output, we know definitely the amount of energy required to keep him in

equilibrium. To this must be added the amount of energy necessary for his growth. But in order to measure the output, the conditions must be always the same and with the child the conditions can be the same only during sleep. Nothing alters the metabolism so much as mechanical work, and when awake the infant is always performing this, and the amount that each one performs is by no means the same and cannot well be estimated, though in the individual case it may be experimentally measured.

Rubner and Heubner dispose of the necessity for keeping the conditions always the same by saying that an infant cannot perform a very measurable amount of work, and that whether he is awake or asleep will not greatly alter the results. Their determinations were always made over prolonged periods, twenty hours out of the twenty-four, with the child sometimes awake, active and crying, and sometimes asleep. Schlossmann's results were obtained in much the same way.

During the last year in Dr. Lusk's laboratory, we made experiments with different children with a calorimeter of the Atwater-Rosa-Benedict type, especially constructed for use with small children and animals, which allows a determination of the heat produced, as well as of the oxygen consumed and the CO_2 excreted, with an error of less than 1 per cent. We could show, first, that it is possible to use for comparison only sleeping hours, and that the increase in metabolism in the waking hours is very great over that in the sleeping. For instance, one boy, J. E. N., who produced during sleep 961 calories per square meter of body surface, calculated for twenty-four hours, produced 1,065 calories, similarly calculated, when awake, and 1,130 calories when crying; and another, W. McG., 1,092 calories when asleep, 1,264 when awake, and 1,514 when vigorously crying.[1] Schlossmann has also shown by determinations of the respiratory exchange on the same infant when asleep and when crying, that the metabolism could be nearly doubled, and that an infant weighing only 5 kilograms, when vigorously crying, expended one-fifth as much energy as a full-grown man at hard labor.

It is obvious, then, that children can be investigated satisfactorily only during sleep. This is unfortunate. It makes the one weak link in the whole chain. We can measure exactly how much energy is given off,

1. The difference in the calculated metabolism of these two children when sleeping I believe to be due to the fact that the formula employed for calculating the surface area does not give correct results with poorly nourished children. The second child, though lighter than the first, was 3.5 cm. longer. Too small a calculated surface area gives too high a metabolism per square meter of surface.

and consequently how much is required, during the absolutely quiet hours, but the extra amount necessary for muscular exertion remains undetermined.

We made many experiments on a healthy well-nourished child 3 months of age, weighing 4.75 kilos, or a little over 10 pounds. He was fed every four hours during the twenty-four, so as to keep his metabolism as uniform as possible. He was put in the calorimeter shortly after a feeding, and his metabolism determined during a period of three hours, but only sleeping hours were used for the averages. It was found that he produced heat which, calculated in the ordinary way per square meter of body surface for twenty-four hours, was equal to 952 calories.[2] I think it would be safe to say that the requirements for an infant completely quiet would be not very far from this, and that from 940 to 975 calories per square meter a day would allow sufficient latitude.

There are no figures with which these may be compared, as the heat produced by children has never before been directly measured; nor have the sleeping usually been separated from the waking hours, as it had not seemed sufficiently important to do so. Rubner's and Heubner's determinations were made, as I have said, over twenty hours in the twenty-four, the children being awake part of the time. It was impossible to continue the experiments throughout the whole twenty-four hours on account of the feeding, and as the most active periods were those shortly before and after feeding and during the bath, much of the effect of the activity was lost. It cannot, therefore, be considered that their twenty hours represent accurately an average of the twenty-four.

Their determinations on different children were 1,054, 973, 1,106 and 1,180 calories per square meter per twenty-four hours.[3] The increase over the figures which we obtained is undoubtedly to be accounted for by the mechanical work that their children performed while awake. The highest figures that they ever obtained, 1,180, were with a very active child who cried much of the time.

If we consider that 940 to 975 calories per square meter of body surface in twenty-four hours is the requisite in sleep, we can only estimate the extra amount required by muscular exertion, and this estimation is extremely difficult, and any errors likely to be enormous. One child differs so much from another in all of his habits; the first may sleep

2. I have used 12.3 as the factor in determining the surface area.

3. Rubner and Heubner used 11.9 as the factor in determining the surface area. I have recalculated their figures, using 12.3.

twenty hours out of the twenty-four and be peaceful, quiet and lethargic, seldom crying, and lying contentedly still; the second may sleep only fourteen or fifteen hours, and when awake may be constantly in motion, crying, struggling, turning and twisting, and in all of these extra hours he demands more energy which, as may be seen from the figures that I have quoted, may exceed the energy-demand in the sleeping hours by 40 per cent. or more.

I have reiterated this in order to emphasize just where the difficulty lies. We know the resting requirements, and we know sufficiently accurately the requirements of growth. Cammerer, by the statistical method, which determines the total food intake and urinary and fecal output, showed that one breast-fed infant retained 15 per cent. of the energy-content of his food for growth, and another, 9 per cent. Rubner and Heubner determined that an artificially fed child retained 12 per cent. for growth. There is apparently a fixed and definite tendency toward uniform growth, and a definite proportion of food is retained for this purpose. Growth is the natural tendency of the child, and energy sufficient for this must be supplied in order to keep him in a normal condition. It appears that 10 to 15 per cent. in excess of the energy required for equilibrium maintenance makes ample provision for growth.

The requirements for growth are thus seen to be relatively small and by no means explain the great difference in the nutritional demands between the infant and the adult, although before the days of exact measurements this was supposed to be the only reason why the young infant required 100 calories, and the adult 35, per kilogram of body weight. Rubner gave the true explanation, that the difference was due to the relatively greater surface area. The smaller the body, the greater the surface area in comparison with another body of similar composition. As the smaller body increases in size, its surface area becomes relatively less and less, and it is for this reason that the requirements of normal children shrink from approximately 100 calories per kilo in the first few weeks of life, to about 70 per kilo at the end of the first year, and not because the rapidity of growth has undergone any great diminution.

There are known, then, the resting requirements of the infant and the extra quantity necessary for growth, but that amount over and above the other that is necessary to compensate for the activities of the waking hours, is as yet to be obtained only by estimation.

I have refrained from approaching my topic from the side of practical application because, at the present time, it does not seem that we are

in a position to utilize the results of the determinations that I have spoken of in an entirely satisfactory way. There are still some additional data that must be supplied, but that it will be possible to do this at some future time I feel reasonably sure.

But the requirements of an infant's nutrition refer to quality as well as quantity. Water must be furnished to the infant in large amount compared with the adult, on account of the infant's great cellular activity. His smaller mass of cells is called on to do almost three times the work that those of the adult have to perform, and they do this to the best advantage only when water is freely provided them.

The salts of potash, sodium, magnesium and calcium are all vitally necessary for the life processes. They are all present in the proper proportion in woman's milk, and are sufficiently represented in any dilution of cow's milk that would be used for any considerable length of time. In the majority of instances, they are in excess in the dilutions given to children, but this excess is not a factor of importance with the healthy child, which is the one that is under consideration. The salts of iron are, however, deficient both in human and, especially, in cow's milk. The large supply of iron present in the liver and other organs of the newly born, may gradually be drawn on, and evidently is intended to be drawn on, during the first year, but this deficiency of iron is one important reason why an exclusively milk diet should not be persisted in too long.

The fats and the sugars are the great providers of energy, and together they furnish approximately 90 per cent. of the body's requirements. To a large extent they may be used interchangeably, and an excess of one may for a time compensate for the deficiency of the other, though not indefinitely. Whatever disturbances these produce, are chiefly recognized by gastro-intestinal symptoms such as vomiting, diarrhea, or soapy stools, and so forth. A deleterious effect of either of these on metabolism, so far as the exchange of energy is concerned, has not been demonstrated.

With the protein it is different. This must be furnished in a digestible and assimilable form to repair the loss by wear and tear and to provide for growth, but beyond a certain point there is a marked disadvantage in giving protein. This is not because the casein of milk is difficult of digestion, but because of the effect on metabolism known as the specific dynamic action of protein. By this action, the total heat production of the person ingesting the protein is raised, often to a marked degree. This increased heat must be disposed of. It may be available for warming the body in cold weather, but is an added source of discomfort and possible

danger in hot weather, when it is difficult to get rid of sufficient heat by radiation; and it may cause a dangerous elevation of the infant's temperature when the heat-regulating mechanism is not fully developed. In addition, the extra ingestion of protein throws additional work on the organs of digestion, and the processes of intermediary metabolism.

Two experiments that I have made indicate this very well. One child, who produced an average of 952 calories per square meter in twenty-four hours, was given, in addition to his regular diet, 15 gm. of nutrose during the twenty-four hours. Nutrose contains nearly 90 per cent. of protein. As a result of this extra protein his heat production rose to an average of 1,051 calories per square meter, or a little over 10 per cent. The metabolism of another child rose from 1,097 to 1,383, or an increase of 26 per cent., with the addition of 30 gm. of nutrose. This represents an undue, unnecessary and, at times, undoubtedly harmful tax on the organism.

It is probable that slightly less protein is required for maintenance and growth in breast-feeding than in cow's milk feeding, owing to the better utilization that can be made of the homologous protein, but the excess required with cow's milk feeding is undoubtedly slight. When feeding a normal child, protein should furnish not less than 8 per cent. and not much more than 10 per cent. of the total energy in the food. When it furnishes 15 per cent., the specific dynamic action becomes noticeable, and when it furnishes 20 per cent., the effect is very marked.

It will be seen, therefore, that in addition to the quantity of the food provided, a proper disposition of the energy among the various constituents is always seriously to be kept in mind.

PROTEIN METABOLISM IN INFANTS AND CHILDREN

HERMAN SCHWARZ, M.D.
NEW YORK

Before going into a general description of nitrogen metabolism it is of the utmost importance to get a general idea of the newer facts known in regard to protein bodies. Protein bodies represent a highly complex organic combination which has become better known through the studies of Hochmeister, Kossel, and especially of Emil Fisher.

The researches of Emil Fisher, Abderhalden, Bergel, Rona and others show that the end-products of the proteins, are the amino-acids obtained by hydrolysis, and are bodies of the normal fat and aromatic series in which the H atom is displaced by an NH_2 group. Of these acids many varieties have been described, of which the better known are glycocoll, alanin, tyrosin, valin, leucin and isoleucin. Whereas the carbohydrate (glycogen) of the body represents combinations of a definite chemical group, the glucoses, and the fats a combination of glycerin and fatty acids, the proteins on the other hand represent many combinations of these amino-acids. We do not as yet classify the proteins by their amino-acid content, if I may use that expression, but according to external properties. Thus we have:

Simple protein bodies.

Complex protein bodies.

The simple protein bodies include the albumins, globulins and the coagulable protein of muscles. These constitute the greater part of the protein in our food and bodies and are what we refer to when we talk off-hand of proteins.

The second group includes mucin, which has a carbohydrate radical attached; the nucleo-albumins, which have a phosphorus group as, for example, milk; hemoglobin, which has an iron group attached, and finally those complex albumins which really perform the functions of our lives, the albumin in the nuclei of the cells, the nucleoproteins, which are made up of purin bodies, phosphorus and carbohydrate groups.

When all these different proteins are ingested, they are split and hydrolyzed by the various ferments in a definite and regular manner.

The pepsin reduces them to albumoses and peptones. The end-products (the amino-acids) are not present in the stomach at all or in but small quantities, for pepsin has the property of splitting up the protein body into these more elementary substances only when they are allowed to remain in contact many hours.

It is the trypsin of the pancreatic juice, and especially the erepsin of the small intestines, by which these bodies are further split up ultimately into the amino-acids. In the course of this transition there is a period when they are not amino-acids, nor yet peptones or albumoses. In this stage they have been called by Emil Fisher polypeptids and he has actually been able by many combinations of amino-acids to manufacture polypeptids. The end-products of the breaking up of the protein molecule are the amino-acids. The number of these acids is considerable, and it is very likely that there are many combinations and thus many different kinds of proteins of which we have not the least idea. The proteins are absorbed in the form of amino-acids and their combinations. The body has actually been kept in nitrogen balance or even in a plus balance by means of feeding experiments with amino-acids.[1] These amino-acids have also been found in the tissues of the body and serous cavities.[2] The proteins, then, are split up by means of ferments into their ultimate component parts, the amino-acids, then absorbed into the body to be reconstructed into various substances and excreted by the kidneys in the form, principally, of urea and ammonia. As yet the intermediary metabolism, the interval between the absorption of the amino-acids from the intestines and their excretion in the urine and feces, contains many a dark spot which needs further investigation. It is to the end-products which as yet are our only guide that I wish to draw attention in this cursory discussion of the nitrogen metabolism in infants and children.

I shall first discuss the total nitrogen, a consideration of the intake necessary at the various ages, and the nitrogen balance. In discussing this question one must first distinguish between the nitrogen metabo-

1. Schittenhelm and Frank: Ztschr. f. physiol. Chemie, 1909, lxiii, 215.

2. Umber: Lehrbuch der Ernährung und Stoffwechselkrankheiten, 1909, Urban and Schwarzberg.

lism in the breast fed and in the artificially fed, and above all, not forget to distinguish between the healthy and the sick infant.

A discussion of the metabolism of the breast-fed child is the most satisfactory and easiest, for by comparing the cases in the literature one is certain that the food given was more or less the same, namely breast milk, whereas in the artificially fed one has the difficulty in correlating different percentages of the various food elements, the different quantities taken, and the uncertainty that one is dealing with normal children.

If we take a number of cases of breast-fed babies (see Table 1) from the literature, as Czerny and Keller and Orgler[2] did, adding some of our own, and observe the amount of nitrogen taken in, we will be immediately struck with the fact that irrespective of the age, the amounts taken in are about the same.

Thus the 3-months-old child of Michel and Peret or the 4-months-old child of Schwarz does not even take as much as the 11-days-old child of Michel, but in contrast to this, the nitrogen in the urine excreted in this 11-days-old child is 0.181 gm. as compared with 0.714 of Michel and Peret and 0.626 of Schwarz. The intake then is about the same but the output is distinctly different, not alone in the urine but also in the feces. The retention is seen to decrease and the output to increase as the infant grows older.

In order to make a comparison of various cases in the literature we must have certain data to go by. These are (1) the amount retained per kilogram body weight per day and (2) the percentage retained as compared with the amount taken in. This latter is called the utilization figure. The first alone would not be sufficient, for if we gave the infant too little, naturally the retention would be too small. A comparison of utilization alone would give us an incorrect picture, for if we gave too much nitrogen, even though a great amount of nitrogen be retained, the utilization would appear small.

It is only by a combination of the amount retained per kilo a day and the utilization, that a proper idea of nitrogen metabolism may be obtained. If these children are arranged according to their ages (see Table 2) and the amount of nitrogen taken in and retained per kilo weight, it will be seen that the amount of nitrogen retained is quite independent of the amount taken in.

TABLE 1.—METABOLISM OF BREST-FED INFANTS, SHOWING NITROGEN INTAKE AND NITROGEN BALANCE

Author	Age of Child	Length of Experiment,	Increase in Weight pro die	Nitrogen				
				Food,	Urine,	Feces,	Balance,	Nitrogen,
	Days	Days	gm.	gm.	c.c.	gm.	gm.	per cent.
Michel[4], I	5	3	27	1.52	0.279	0.066	+1.17	77.2
Michel, II	11	3	40	1.87	0.181	0.090	+1.59	85.5
Michel, III	5	4	37	1.462	0.217	0.138	+1.10	75.7
Schwarz[5], IV	4	3	10	1.232	0.188	0.050	+0.994	73.
	Mos.							
Keller[6], VIII, IV	2	5	28	1.875	0.787	0.244	0.843	45.
Michel[7] and Peret[5]	3	3	29	1.675	0.714	0.176	0.785	46.9
Schwarz	4	3	25	1.337	0.626	0.241	0.570	42.6
Schwarz	4	2	12	1.623	0.701	0.164	0.785	46.3
Rubner[8] and Heubner	5	3	85	1.99	1.13	0.40	0.46	23.1

3. Orgler: Ergebnisse der Inneren Medizin und Kinderheilkunde.
4. Michel: Recherches sur la nutrition normal du nouveau-ne. Obstetrique, Par., 1896.
5. Unpublished. Premature weight 1.8 kilo.
6. Keller: Arch. f. Kinderh., 1900, xxix, 1.
7. Michel and Peret: Obstetrique, Par., 1899.
8. Rubner and Heubner: Ztschr. f. Exper. Path. u. Therap., 1905. i.

TABLE 2.—AMOUNTS OF NITROGEN TAKEN IN AND RETAINED ACCORDING TO AGES

Author*	M I	M II	M III	Schwarz	K VIII	M and P	Schwarz	Rubner and Heubner
Intake pro kilo N...	0.407	0.425	0.545	0.685	0.430	0.354	0.286	0.205
Retention pro kilo N.	0.314	0.343	0.410	0.552	0.194	0.156	0.143	0.048

*The cases are the same as those referred to in Table 1.

If we compare K VIII with M II we see that with similar intake we have 194 mg. retained in one instance and 343 mg. in the other. If we compare the amount retained and their ages it will be seen that the amount of retained nitrogen is dependent on the age, so that a 14-days-old child retains the most and the 5-months-old child the least. Therefore the amount of nitrogen per kilogram weight required in infancy is apparently about the same, but the amount retained and its proportion to the amount taken in, is according to the age.

Grouping a number of these cases roughly together according to age as shown by Orgler,[3] we have an excellent idea of the utilization of nitrogen in infancy.

Age	Up to 14 Days	2 to 3 Months	5 Months
Retention	0.351	0.153	0.048
Utilization	78.3	40.8	23.1

The nitrogen metabolism of the first few days of life shows such distinctive characteristics that I have deemed it better to discuss this separately and collect the available material in one table. Langstein and Nieman showed that there is a negative nitrogen balance during the first few days when the baby is fed on woman's milk pumped from a well-established lactating breast. In their first case the balance was negative for the first four days; in the second case for the first two days; third case for the first two days, and in the fourth case, a premature baby, it was negative for the first eight days of life. In an infant of Schloss and Crawford's, fed on colostrum, the intake of nitrogen was 1.5 gm., and about 1.1 gm. was excreted in the urine and feces, with a utilization of 26 per cent. Schwarz' case, that of a premature infant, beginning from the third day up to the seventh day of life, can hardly be brought under this heading, for it was not controlled from birth. It was fed on woman's milk and showed a retention of over 2.0 gm. of nitrogen during this time, and a utilization of 77 per cent.

TABLE 3.—NITROGEN METABOLISM IN THE NEW-BORN

Author	Weight, Beginning to End of Experiment	Age during Experiment, days	Food Given	Intake N, gm	Urine N, gm.	Feces N, gm.	Balance N Retention, gm.	Utilization per cent. N, gm.
Schloss and Crawford[9]	....	1-3	Colostrum	1.512	0.598	0.520	+0.394	26.0
Schloss and Crawford	....	3-6	Colostrum	2.883	0.926	0.141	+1.818	63.0
Schloss and Crawford	....	6-9	Colostrum	2.783	0.922	0.139	+1.724	61.9
Schwarz[10]	....	3-7	Woman's milk	3.388	0.547	0.142	+2.698	99.0
Birk[11]	....	1-5	Colostrum	2.886	1.412	0.524	+0.951	33.
Birk	....	....	Woman's milk	0.696	0.891	0.151	—0.346	0.
Langstein and Nieman[12]*	....	7-10	Woman's milk	1.728	0.603	0.186	+0.939	54.
Michel[4] V	35.50	4	Woman's milk	1.808	0.351	0.061	+1.34	73.0
Michel I	37.30	5	Woman's milk	1.52	0.279	0.066	+1.17	72.2
Michel III	26.80	5	Woman's milk	1.46	0.217	0.138	+1.10	75.7
Birk[13]	30.34	3	Cow's milk	0.897	0.437	0.397	+0.063	7.0
Birk	35.30	5	Cow's milk	3.2	2.116	0.096	+0.993	31.0
Birk	....	0-4	Cow's milk	1.339	1.326	0.620	—0.607	0.
Birk	....	0-3	Cow's milk	0.599	0.378	0.147	+0.075	12.5

*Intake and output for four days from seventh to tenth, inclusive, were added together in order to get above figures. First five days gave a negative N balance.

9. Schloss and Crawford: Am. Jour. Dis. Child., i, 203.
10. Schwarz: Case Rogers—Premature, 3 days old.
11. Birk: Monatschr. f. Kinderh., ix, 180, No. 11.
12. Langstein and Nieman: Jahrb. f. Kinderh., lxxi, 604.
13. Birk: Monatschr. f. Kinderh., x, No. 1.

Birk's patient—Case I—was fed on colostrum in a five days' experiment, during which there was a physiologic loss from 3,980 gm. to 3,760 gm. In spite of this there was a retention of 0.951 gm. nitrogen, a utilization of 33 per cent. In a second case there was a retention of nitrogen from the second day of life. His third patient, fed on woman's milk from birth, showed a loss of nitrogen. We see here an interesting physiologic fact, that with a loss of weight there may be a retention of nitrogen in the patients fed on colostrum, and a loss of nitrogen when fed on woman's milk. This shows the value of colostrum, for in Langstein's case this loss is ascribed to a breaking down of protein in the tissues. In two of Birk's patients fed on cow's milk the results varied somewhat, for in Case I there was a loss of 606 mg. of nitrogen and in the second case a retention of 75 mg. of nitrogen. The utilization of the nitrogen in the cases in this table differs somewhat from the general rule given by Orgler previously in being considerably less. This is in part due to the fact that in some of the cases the first few days with low utilization of nitrogen are included with the later days of higher utilization, as might have been done if Schloss' periods had not been separated as shown in the tables. Thus, in the first three days the utilization was 26 per cent.; then 63 per cent., which is nearer to the figures obtained by Michel and Peret. Birk ascribes the low utilization in the babies fed on cow's milk to the large excretion of nitrogen in the urine, which in Michel's cases was one-sixth and one-seventh of the intake, while in the cow's milk babies it was as high as two-thirds of the intake. This he regards as a fundamental difference between the two types of feeding. Yet in Schloss' case during the first three days, 30 per cent. of the nitrogen intake was excreted in the urine, and in Birk's Case I, fed on colostrum, 50 per cent. of the nitrogen appeared in the utilization. From the foregoing it is clear that nitrogen utilization in the new-born needs considerable more investigation.

Before taking up the nitrogen metabolism of the artificially-fed child, it is important to know the effect in the same child of increasing the various food elements in the mixture.

As shown above, in the breast-fed child the amount of nitrogen excreted in the urine is not constant and is of no value except as compared with the intake, being 11 per cent. in Michel's[4] 5-days-old child, and 42 per cent. in Michel and Peret's[7] 3-months-old child. So also the

amount of nitrogen in the stools, in the breast and artificially fed varies according to the age and the character of the food. The stools present a special problem, for here the nitrogen may be derived from the food, the intestinal secretions, bacteria or epithelium. The nitrogen content of the stool can be increased by changing the character of the food, thus causing an increased secretion, or perhaps poor assimilation or resorption of the food nitrogen. Because nitrogen is added to the food and an increased amount of nitrogen is excreted in the stools, does not necessarily mean that this nitrogen came from the food, for there may have been more intestinal secretion, epithelium or bacteria excreted. In Schlossman's case Kriesch, as quoted by Orgler,[14] the child excreted 1.22 gm. nitrogen in the feces, with an intake of 6.5 gm. of nitrogen, whereas with an intake of 10.05 gm. nitrogen, excreted only 1.119 gm. Child M IV in Orgler's experiment[15] excreted 0.62 gm. nitrogen in the feces with an intake of 8.1 gm. nitrogen. At another time this infant received 3.3 gm. nitrogen and excreted 0.61 gm. nitrogen, a difference of only 0.01 gm. nitrogen. In one of my experiments a breast-fed baby getting 1.6 gm. nitrogen excreted 0.164 gm. nitrogen in the stools; at another time receiving 1.25 gm. nitrogen, excreted 0.346 gm. or three times the former amount with the same intake. The amount of nitrogen in the food then has very little influence on the nitrogen in the feces.

In hunger there is always a small amount of nitrogen in the stools. A patient of Keller's, examined while on a water diet, excreted 0.0716 gm. nitrogen, or 7 per cent. of the dried feces. In Orgler's case[15] the stools contained 5 per cent. nitrogen (dried feces). In my cases with an intake of 1.47 gm. nitrogen and an excretion of 0.15 gm. nitrogen in the stool, there was 4.5 per cent. nitrogen in the dried feces. In another instance with an intake of 1.252 gm. nitrogen there was an excretion of 0.346 gm. nitrogen in the feces, or 4.3 per cent. of the dried feces. This percentage of nitrogen (about 5 per cent.) to dried stool is fairly constant. If a nitrogen-free diet succeeds a water diet there will be an increase in nitrogen in the feces. What is most interesting is, that if a little flour, which in itself contains but very little nitrogen, is added to nitrogen-free food, there will be a great increase in the nitrogen excretion in the feces. Such an instance is a case of Rubner and Heubner.[16] With a diet of flour containing 1.02 gm. nitrogen there was 0.45 gm.

14. Schlossman: Arch. f. Kinderh., 1904, xl, 1.
15. Orgler: Monatschr. f. Kinderh., 1908, p. 135.
16. Ztschr. f. Biol., 1899, xxxviii, 315.

nitrogen in the stools—almost 50 per cent. of the intake. Therefore, as shown by Orgler, the resorption or the difference between the nitrogen intake and that found in the stools is of very little value, and an increase of protein in the food may have no effect on the nitrogen of the feces.

In the adult when in health and taking the proper amount of food there is just a nitrogen balance, but in infancy, in health, there is a marked retention. This is the great difference in their nitrogen metabolisms, for the latter is a growing organism and needs its nitrogen for its increase in weight and growth. It is very difficult to bring an infant into a state of nitrogen equilibrium, in which he will be excreting as much as he takes in. This can be done by reducing the protein intake sufficiently. This will, however, cause a diet to be given which is caloric-ally entirely below the requirements necessary to retain weight. If we proceed now to add protein, the infant will immediately begin to retain nitrogen, although the food values may be very much below the required amount. This explains the phenomenon of nitrogen retention and no gain in weight. The infant adds to its growth and not to its weight.

To illustrate the effect of the addition of fat to the food, I reproduce in part a table of Orgler's (Table 4).

TABLE 4.—SHOWING THE EFFECT ON NITROGEN BALANCE OF THE ADDITION OF FAT TO THE FOOD

Food	Nitrogen in Food, ... gm.	Urea N, ... gm.	Feces N, ... gm.	Balance, ... gm.	Nitrogen utilization per cent.
Freund I.,[17] Buttermilk	3.389	2.446	0.278	0.665	19.6
Buttermilk and butter	3.047	2.144	0.311	0.592	19.4
L. F. Meyer,[18] 200 c.c. milk, 800 c.c. barleywater, 16.5 gm. casein, 20 gm. sugar.	3.55	1.799	0.256	1.417	42.2
20.0 gm. same and butter ...	3.6296	1.93	0.202	1.45	40.

From Table 4 it will be seen that when buttermilk alone is given, with a nitrogen content of 3.387 gm. there is a utilization of 19.6 per cent. If butter is added, we have the same utilization of nitrogen. L. F. Meyer's[18] case illustrates the same thing. So that we may conclude that the addition of fat to the food does not save nitrogen and the utilization is the same.

17. Freund: Zur Wirkung der Fettdarreichung auf dem Säuglingsstoffwechsel, Jahrb. f. Kinderh., 1905, lxi, 36.

18. L. F. Meyer: Biochem. Ztschr., 1908, xii, 422.

The influence of carbohydrates on the nitrogen metabolism is very marked. From Table 5 it will be seen that when a mixture one-half each of milk and water is given, the child retains 0.2 gm. of nitrogen with a utilization of 9.9 per cent. and on giving the same mixture with the addition of malt in the form of malt-soup we have a retention of 0.4 gm. of nitrogen and a utilization of 17 per cent. This action of the carbohydrates, however, does not work in instances in which the children do not stand sugar well, as shown in an experiment on Orgler's Baby O,[19] in which the addition of sugar caused a marked loss of nitrogen. The saving of nitrogen by sugar is caused partly by the fact that the child does not need to draw on its protein if it has plenty of sugar.

TABLE 5.—(FROM ORGLER). NITROGEN BALANCE AND NITROGEN UTILIZATION ON DIETS OF MILK AND WATER AND MALT-SOUP

Food	Food N, c.c.	Urine N, c.c.	Feces N, gm.	Balance, gm.	Utilization per cent.
½ milk and water	2.672	2.027	0.380	6.264	9.9
Malt-Soup	2.3443	1.4963	0.431	0.417	17.8

This cannot be the only cause, for it can be shown that if a very small amount of barley diluent is added instead of water the retention is increased out of all proportion to the very slight increase of carbohydrate and nitrogen in the barley. The utilization is also markedly increased. Just what this is due to is not known.

The relation of the mineral metabolism to the nitrogen metabolism, according to Orgler, is fairly constant. Designating the amount of ash retained as 1.0, the relation of nitrogen to ash will be seen in Table 6, taken from Orgler.

TABLE 6.—SHOWING THE RELATION OF NITROGEN TO ASH

Michel[4] I	2.1:1
Michel II	1.8:1
Michel IV	1.6:1
Michel and Peret	1.4:1
Rubner and Heubner	1.7:1

This is not the case in artificially fed infants and is especially important in sick children, for whenever alimentary disturbances occur there is a marked divergence from the above.

In a consideration of the nitrogen metabolism of the healthy artificially fed, all the above-mentioned factors must be taken into consider-

19. Orgler: Jahrb. f. Kinderh., 1908, lxvii, 383.

TABLE 7.—SHOWING NITROGEN INTAKE, RETENTION AND UTILIZATION IN BREAST-FED AND ARTIFICIALLY FED INFANTS

Author	—— Keller —— (KVIII)		—— Orgler —— I		—— Orgler —— II		—— Orgler —— III		——Schwarz——	
	Breast Fed	Bottle Fed	Breast Fed	Bottle Fed	Breast Fed	Bottle Fed	Breast Fed	Bottle Fed	Breast Fed	Bottle Fed
Intake, gm.	0.320	0.454	0.221	0.379	0.234	0.498	0.191	0.425	0.295	0.35
Retained, gm.	0.194	0.155	0.076	0.120	0.108	0.148	0.053	0.154	0.144	0.20
Utilization, per cent.	45.	34.	34.	31.	45.4	29.	27.9	36.4	48.8	58.8

ation and one must be sure that the child is absolutely healthy and gaining weight regularly. It is important in the first instance to be oriented concerning the utilization and intake with breast and artificial feeding in the same child in order to determine whether the utilization of nitrogen is the same or better in the one method of feeding than the other. For this purpose Orgler has three cases in sick infants and only one in a healthy breast baby. To this we can add one case in a breast child which was apparently healthy, and was used because its mother had a nephritis and was excreting large quantities of albumin in her urine. The infant also had a faint trace of albumin.

In Table 7 these cases are tabulated. It was unfortunate that in Keller's case the child while on the bottle did not get enough calorically, yet the utilization was almost as good as when on the breast. In comparing Orgler's Case III and Schwarz' case it will be seen that the retention and utilization while on cow's milk may even be better than with breast milk if the artificial feeding is properly conducted. In a comparison of healthy bottle babies to other breast babies of the same age it can be said that the retention and utilization is at least as good. The resorption is also as good in artificial feeding as in the breast feeding, as shown in a case of Orgler's[20] in which an infant getting five feedings a day of woman's milk had resorption of 74.8 per cent. of intake; on two feedings of breast milk and three of cow's milk the resorption was 78.3 per cent. and on a cow's milk mixture calorically sufficient the resorption was 82 per cent.

In the sick infant, the conditions in breast or artificially fed infants are harder to compare, for here the unit of comparison, the kilo, is usually less than in normal children of the same age, and this fact necessitates a comparison with younger children. It is remarkable how much nitrogen these infants will retain while in their convalescence from intestinal disturbances. This pertains also to the artificially-fed child.

Orgler's[21] conclusions concerning nitrogen utilization might well be repeated.

1. Healthy artificially-fed infants show similar or even better figures of nitrogen retention than healthy breast-fed babies of the same age.

2. Retention in the sick artificially-fed child is as good as in the sick breast-fed child.

20. Orgler: Monatschr. f. Kinderh., 1908, vii, 135.
21. Orgler: Ergebnisse der inneren Medizine und Kinderheilkunde, ii, 509.

3. Healthy infants often show better figures for retention when given a proper cow's milk mixture than on the breast.

4. The utilization of nitrogen may be as good or even better in the artificially fed than in the breast fed.

Let us consider for a moment how the functions of nitrogen differ in the adult and in the child.

1. Nitrogen repairs waste; makes good the daily wear and tear of the protein constituents of the tissues, used up in the performance of their functions. Of course this is equally important to both child and adult, but in the latter it constitutes most of its utility, and in arranging the adult dietary the protein need which shall subserve this function is alone imperative. In infants this minimum protein need, on account of reasons given before, cannot be accurately determined, but in some experiments it seems to run from 0.2 to 0.45 gm. nitrogen during the first fourteen days of life. In an older child a nitrogen equilibrium was struck when given 0.9 gm., being furnished with sufficient calories for its needs by the addition of carbohydrates.

2. Nitrogen adds to the body substance. This deposit or storage of nitrogen plays a secondary rôle in adults, but in children is of prime importance. In adults, under usual conditions, nitrogen is not stored. Any excess administered is split up, burned and eliminated. Only in the hypertrophy of muscles put to special activities, in pregnancy, in convalescence from wasting diseases and after prolonged fasting does such a deposit obtain. In infants and growing children a large part of the nitrogen ingested is added to the body bulk in response to the imperative demand of the impulse of growth. So insistent is this demand that an infant can store nitrogen even when the calories of the food are insufficient. This fact accounts for the common observation that a child will increase in length, though the gain in weight is not essential. In an adult a diet of insufficient caloric value leads to protein loss.

3. The third function of protein is to furnish heat and energy to the body. The heat value of protein is about the same as that of the carbohydrates. Each gram of either substance when completely combusted gives rise to 4.1 calories.

It is not, however, a function for the performance of which the human body looks to protein, but rather to fat and carbohydrates. Moreover, it is not an economical form of fuel when so used, owing to what

is termed its "specific dynamic action," some 28.6 per cent. of its value is given off as free heat, leaving only 71.4 per cent. available for the purposes of cell life.

In infants this function of protein plays a small part, especially in natural feeding.

In early life, then, protein is used to repair waste; then to be stored to the limit of the storage capacity of the body; then to furnish energy and be eliminated in the urine.

The sparing of nitrogen built into the body and the storage of nitrogen brought to the body are greatly influenced by the constitution of the food as a whole. Indeed, the art of feeding in infancy, and quite as much in morbid conditions in adult life, depends on this appreciation of the effect of one food stuff on another in the metabolism of each.

As previously stated, the protein taken in is reduced to its ultimate amino-acids, then built up again and excreted mostly in the form of urea and ammonia. It is to a discussion of these, as they make up a part of the total nitrogen in the urine, that we will now turn our attention. It is customary to quote the figures of various constituents of the nitrogen (nitrogen partitions) in the urine, in two ways: first, in actual milligrams excreted in twenty-four hours, and secondly in the amount of each substance as compared with the total amount of nitrogen in the urine.

This urea nitrogen and the ammonia nitrogen constitute the largest part of the nitrogen in the urine. These again, subtracted from the total nitrogen, leave a residue which was previously commonly called the undetermined nitrogen. This undetermined nitrogen is becoming more and more subdivided as we discover new methods of determining quantitatively the products of protein metabolism. At present it can be subdivided into the uric acid nitrogen, purin body nitrogen, creatinin and creatin nitrogen. When all these and the urea and ammonia nitrogen are subtracted from the total nitrogen in the urine, there is still a fraction which is in reality the undetermined nitrogen and is practically identical with the amino-acid nitrogen.

UREA

The formation of the gross urea nitrogen (urea and ammonia nitrogen) excreted in the urine is still an unsettled point. There are probably many ways in which it is formed in the body. That urea is a synthetic product of the amino-acids was long ago definitely established

by Schultzen and Nenki[22] and it has been proved that at least one amino-acid, really a diamino-acid, namely arginin, found in the intestine, can be inverted into urea by means of the ferment arginase (Kossel and Dakin[23]). This, however, does not represent all of the urea excreted in the urine. The most probable theory is that the amino-acids have their NH_2 groups split off by desamidating ferments, taken to the liver by the portal circulation, and the liver synthetizes some to urea, the remaining portion being excreted as ammonia. The gross urea therefore represents very probably the desamidating capacity of the organism.

The urea nitrogen according to Morner and Sjoqvist makes up 72 to 76 per cent. of the total nitrogen excreted in the urine. In a year-old child Camerer found the urea nitrogen 72 to 76 per cent. of the total nitrogen, and in a 5-months-old breast baby 83 per cent. of the total nitrogen. In a case of mine a 5-months-old breast baby excreted 0.5 gm. a day, or 72 to 75 per cent. of the total nitrogen, and when put on the bottle this child excreted 0.6 gm. per day or 78 per cent. of the total nitrogen. L. F. Meyer and Ritschel state that the urea coefficient, that is, the percentage of urea nitrogen to total nitrogen, is from 60 to 80 per cent. Hoobler[24] in a presumably normal bottle baby 9 months old, found the urea excretion 52 per cent. when fed on low fats, and 44 per cent. on high fats. This latter is probably due to the fact that there was a compensatory increase in the ammonia nitrogen. In an older child, 5 years of age, the urea nitrogen excretion was found by Schwarz[25] to be 6 to 7 gm. per day, or 87 per cent. of the total nitrogen. According to Folin[26] the amount of urea excreted depends on the nature of the diet. He showed that in cases with a rich nitrogen diet such as eggs and milk, the urea nitrogen can be as high as 87 per cent. and with a nitrogen-free diet may be as low as 60 per cent.

Vogt[27] showed that in acute gastro-enteritis the urea may be as low as 36 per cent. This, however, is not characteristic of acute gastro-enteritis, for a low urea was also found in patients with marked malnutrition without acute intestinal disturbances. They did not seem to do well either on woman's milk or on cow's milk, probably due to an intol-

22. Schultzen and Nenki: Ber. d. deutsch. chem. Gesellsch., 1869, ii, 566.
23. Kossel and Dakin: Ztschr. f. physiol. Chemie, 1904, xli, 32.
24. Hoobler: Arch. Pediat., 1910, xxvii, 856.
25. Schwarz: Jahrb. f. Kinderh., 1910, lxxii (Series 3, xxii, part 5).
26. Folin, O.: Am. Jour. Physiol., 1905, xiii, 45 and 116.
27. Monatsch. f. Kinderh., viii, No. 2.

erance to fat. This effect of increased fat, or perhaps an intolerance to fat, is shown in Hoobler's case when put on a high fat mixture. Does this low urea excretion mean a disease of the liver? That this is the case in some instances is demonstrated in acute yellow atrophy and phosphorus poisoning in which there is a markedly decreased excretion of urea nitrogen. In gastro-enteritis, however, according to Thiemich,[28] quoted from Vogt, the liver is damaged only in a small percentage of the cases and even in chronic nutritional disturbances there is no great destruction of liver parenchyma. Yet the histologic changes may have no bearing on the ability of an organ to perform its chemical functions.

UNDETERMINED NITROGEN

Before discussing the ammonia nitrogen, I will touch on the question of the undetermined nitrogen in the urine. As stated before, this figure is obtained roughly by adding the ammonia nitrogen to the urea nitrogen and subtracting this from the total nitrogen.[29] In this undetermined nitrogen is included uric acid nitrogen, creatin and creatinin nitrogen, and purin body nitrogen, all of which will be discussed later. This nitrogen is unaffected by the amount of nitrogen ingested and is supposed by Folin and others to be the nitrogen product of a metabolism apart from the other—an expression of the intermediary metabolism. Because of the decrease in the urea nitrogen mentioned above, we have an increase in the undetermined nitrogen, provided the ammonia nitrogen remains constant. Inasmuch as these children with acute and chronic intestinal disturbances are in a state of under-nutrition, it might be said that this diminished urea and high undetermined nitrogen is due to hunger. In adults and in children also, hunger decreases the urea nitrogen, it is true, but there is such a marked increase in the ammonia nitrogen, that when both are added together and subtracted from the total nitrogen we have no increase in the undetermined nitrogen. Vogt examined the nitrogen partition in the urine of new-born infants and was able to find two distinct classes; one with a percentile decrease in the urea and a corresponding percentile increase in the undetermined nitrogen; the other with a high urea and a low undetermined nitrogen. He found, for instance, 46 per cent. urea nitrogen and 44 per cent. undetermined nitrogen as compared with the total nitrogen. In other cases 81 per

28. Thiemich: Beitr. z. path. Anat. u. z. allg. Path., xx, 179.

29. I have done this in this portion of my paper because Vogt discusses the nitrogen partitions in the new-born in this manner.

cent. urea nitrogen and 11 per cent. undetermined nitrogen. Whether this is due to an increase in the uric acid excretion in the one, or to a diathesis, it is impossible at the present moment to say. The increase or decrease in uric acid excretion, however, should not affect the urea; it might, though, make up the greater part of the undetermined nitrogen, and therefore not mean a decreased excretion of the amino-acids in the urine. It is interesting to note that in Hoobler's case on low and medium fats, the undetermined nitrogen was 4.6 per cent. of the total nitrogen, whereas on high fats there was 11.5 per cent. undetermined nitrogen in the urine. Whether this high undetermined nitrogen means a disability of the liver or other organs to form urea from amino-acids, is still an open question. The urea excretion in the many pathologic states in infancy has not been investigated. It would seem especially important to know the excretion of urea in various types of malnutrition. In three cases of rachitic dwarfism Schwarz[30] found the excretion of urea normal as compared with a healthy child.

AMMONIA NITROGEN

Since the discovery by Keller[31] that the ammonia nitrogen in the urine of children suffering from alimentary intoxication is greatly increased, intense interest has been manifested in the ammonia excretion in the infant's urine. The ammonia nitrogen co-efficient, that is, the percentage of ammonia nitrogen to total nitrogen, has been the subject of considerable investigation. In a five months' old breast baby Camerer found this co-efficient to be 7.7 per cent.; Keller, 7.7 to 12 per cent. Meyer and Langstein[32] claimed that figures under 10 per cent. are normal. Amberg and Merrill[33] found the ammonia nitrogen co-efficient in breast babies during the first few weeks of life to be from 4 to 12 per cent. During hunger the ammonia output in the urine increases and must not be confounded with an acidosis. Meyer and Langstein have noticed this increase already on the second day of hunger. Folin[26] states that a decrease in the nitrogen intake enough to show a decrease in the nitrogen output in the urine will give an increase in the excretion of ammonia in the urine. Therefore, the ammonia excretion in the

30. Schwarz: Jahrb. f. Kinderh., 1910, lxxii, 724.
31. Keller: Jahrb. f. Kinderh., 1897, xliv, 55.
32. Meyer and Langstein: Jahrb. f. Kinderh., 1906, liii, 30.
33. Amberg and Merrill: Jour. Biol. Chem., 1907, iii, 311.

normal infant depends on the amount of nitrogen in the food. It has been generally understood that an increase of fat in the food alone caused an increase in the ammonia output. This was shown not to be absolutely the case by Amberg and Merrill,[34] for if the proteins are increased with the increase in the fat there will be no increase in the ammonia output. It depends more or less on the relationship of the fat to the protein. They have shown in a breast-fed baby that if this relationship were kept at 3 to 1 the ammonia output was only 8 per cent. If, however, the fat was increased and not the protein, the ammonia excretion went up to 18 per cent. In Hoobler's[24] case the ammonia nitrogen went up from 2 per cent. on a low fat to 15 per cent. on a high fat mixture, but in this experiment the protein remained about the same, only the fats being increased. From the foregoing it is easily seen that one must be very careful in judging an acidosis by the amount of ammonia excreted. However, the excretion of ammonia in the cases described by Keller went up to 30 or 40 per cent. of the total nitrogen. This is undoubtedly due to an acidosis. It might also be due to a disturbance in the formation of urea, but Keller[35] found that by giving amino-acids such as glycocoll, leucin, and asparagin, there was no relative diminution in the excretion of urea. Pfaundler,[36] on the other hand, thought it might be due to a disturbance in the liver and the formation of urea, on account of the fact that there was a diminished ability of the liver to oxidize salicyl aldehyd. However, the later researches of Stemitz, Keller and Freund proved it to be beyond a doubt due to an acidosis, the increased excretion of alkali taking place through the feces and the ammonia used to neutralize the acids formed.

NUCLEOPROTEIN.

Before taking up a consideration of the remaining nitrogen constituents of the urine it is important to know something of the breaking down of the nucleoprotein from which a greater part of this nitrogen comes. This nitrogen (uric acid, creatinin, etc.), as contradistinguished from the urea nitrogen, has absolutely no relation to the protein intake. Folin advanced the theory that there are two metabolisms going on, an

34. Amberg and Merrill: Jahrb. f. Kinderh., lxix.
35. Keller: Centralbl. f. allg. Pathol. u. path. Anat., 1898, ix, 739.
36. Pfaundler: Jahrb. f. Kinderh., liv, 247.

exogenous and an endogenous. In the exogenous metabolism the organism takes care of the entire intake of nitrogen, with the exception of a small part which goes to the repletion of that nitrogen lost in the endogenous metabolism. This endogenous metabolism is, however, affected by the nucleoprotein intake and it is to this we must now turn our attention.

As stated in the beginning of the discussion, the nucleoproteins are a class of complex proteins and are found in food richly supplied with cells. They are made up of proteins and nucleic acids: Protein *loosely* combined, and protein very *closely* combined, with the nucleic acids, so that when they are taken into the stomach, the pepsin takes the loosely combined protein, forms peptones, albuminoses, polypeptids, and amino-acids. What is left is nucleic acids plus the closely combined proteins, together commonly called nucleins. The trypsin of the pancreatic juice then splits off the protein from the nuclein, and nucleic acids are left. These acids are, no doubt, also split up, but as yet there is only one known ferment that can do so, namely, nuclease, discovered by Sachs[37] in 1905. The pancreatic juice in addition has the property of changing the nucleic acids so as to render them more easily split up. They are broken up in the intestinal wall but not in the lumen of the intestines. Here they are resorbed, but just where they are changed into nucleoprotein of the body is unknown. Perhaps they are taken by the blood stream to the various organs, there combining with the nucleoprotein of the blood, forming the nucleoprotein of these organs. A portion of the nucleic acids is broken down by the intestinal bacteria, for purin bodies are found in the stools.[38] They are derived, no doubt, from epithelium and bacteria.

Nucleic acids when split up result in the following:

1. Purin bases; guanin, adenin, xanthin and hypoxanthin.
2. Pyrimidin bases: thymin, cytosin, uracil.
3. Carbohydrate group (hexoses).
4. Phosphoric acid.

Guanin, a purin base, can be converted into xanthin by means of a ferment, and this in turn can be converted into uric acid. Adenin, on the other hand, can be changed into hypoxanthin by means of a ferment,

37. Sachs, Fritz: Ueber die Nuclease, Ztschr. f. physiol. Chem., 1905, xlvi, 337.

38. Kruger and Schittenhelm: Ztschr. f. physiol. Chem., 1905, xlv; 1902, xxxv, 153.

this again into xanthin and then into uric acid.[39] This shows the close connection which these nucleoproteins or nucleic acids have with the formation of uric acid. Jones thinks these changes are due to different ferments (guanase and adenase), but Schittenhelm believes them to be due to the same ferment.

URIC ACID

Uric acid represents the direct metabolism of the nucleoproteins in the food, and it is shown that its excretion is in direct relation to the amount of these bodies ingested. However, if a patient is given a nucleoprotein, or, as it is called, a purin-free diet, he will still excrete a small quantity of uric acid, which is exceedingly constant for the same individual. Burlan and Schur,[40] who first pointed this out, called this the endogenous uric acid. The increased excretion found on giving purin bodies they called the exogenous uric acid. Now, just where does this endogenous uric acid come from? Burean[41] showed that during muscular exercise there is an increased excretion of purin bases in the urine, and soon after of uric acid. He thinks, therefore, that it is formed in the muscles. But it has been shown by Schittenhelm that part of the uric acid thus formed can be destroyed by a ferment which he called the "urikolytic ferment." Therefore, the amount of uric acid excreted is not necessarily all that is formed in the body. If decreased or increased in the urine it can only be interpreted as to whether more is destroyed or less formed. If the former is the case, then the substances into which uric acid is split up should be increased in the urine. Some of these substances, such as glycocoll, oxalic acid and allantoin have been found. A discussion of these, however, would take us too far afield. Yet a search for these substances is of importance as allantoin has been found in the urine of the newly-born by Gusserow.[42]

The excretion of uric acid is especially interesting in the infant, for it receives a food which is purin-free, except during the first few days of life. In order to add nucleoprotein to its body, then, it must

39. Werner, Hugo: Ergebnisse der Physiologie der Harnsäure. 1902, i, Abt. p. 555; Schittenhelm, A.: Die Purinkörper, etc., Ztschr. f. Stoffwechs. u. Verdauungskr., 1904, v, 226; Burean, Richard: Med. Klin., 1905, i, 131; ii, No. 19-21; Mendel: Harvey Society Lecture, Feb. 10, 1906.

40. Burean, Richard, and Schur, Hyman: Arch. f. d. ges. Physiol. (Pflüger's), Bonn, 1900, lxxx, 241; 1901, lxxxvii, 239; Rockwood: Am. Jour. Physiol., 1905, xii, 38.

41. Burean: Ztschr. f. physiol. Chem., 1905, xliii, 494.

42. Gusserow: Arch. f. Gynäk. Berl., 1872, iii, 270.

be able synthetically to produce these, and it has been shown by experiment on the lower animals that the organism is able to produce nucleoproteins even if kept on a purin-free diet from birth. According to Orgler[43] a breast-fed infant excretes 30 to 40 mg. of uric acid; an artificially-fed one, 70 to 90 mg., the retention being greater in the breast-fed. It makes up about 3 to 5 per cent. of the total nitrogen in the urine.

TABLE 8.—URIC ACID EXCRETION IN INFANTS. TOTAL IN THREE-DAY EXPERIMENTS (ORGLER)

Food	Uric Acid, ... gm.	Total Purin Bodies, gm.	Uric Acid, ... gm.	Total Purin Bodies, gm.
Breast milk	130.1	137.0	125.	159.3
Cow's milk	201.2	244.6	247.2	288.3
Increased per cent.	54	78	99	82

As noted before, an increase in the nitrogen intake with a purin-free diet does not increase the uric acid excretion. The addition of carbohydrate to the food, however, according to Orgler, reduces the amount of uric acid excreted and there is an increased retention. If this increase in the carbohydrate is continued, the amount of uric acid excreted will increase slightly, but not to the quantity that it was at the beginning of the experiment. As observed before, the addition of carbohydrate to the diet causes an increased retention of nitrogen and with this increased retention of nitrogen an increase in the retention of uric acid, and protein is added to the body with a resulting increase in weight and growth. Were this retention of nitrogen any better in the breast-fed than in the artificially-fed child this might explain the small excretion of uric acid in the former and a correspondingly greater and more steady increase in weight in the breast-fed. Inasmuch as this is not the case one cannot ascribe the greater protein increase to this fact. The nucleoprotein however has a phosphorus and iron group, and it has been shown by Krasnogorsky[44] that the absolute retention of iron is much better in the breast-fed than in the artificially-fed. Orgler thinks this may be the reason that more purin is added to the body of the breast-fed baby than to the one artificially fed, even though the retention of nitrogen is the same. Concerning the uric acid output in

43. Orgler: Ueber Harnsäure ausscheidung im Säuglingsalter, Jahrb. f. Kinderh., 1908, lxvii, 383.

44. Krasnogorsky: Jahrb. f. Kinderh., 1906, lxiv.

the new-born, conditions are somewhat different. Schloss and Crawford[9] have shown that the output is absolutely and relatively high, being greatest in the first three days of life. It is out of all proportion to the amount of purin bases in the colostrum and is greater when the cord is ligated late. They found the excretion to vary from 60 to 100 mg. of uric acid nitrogen per day the first four days of life, 30 to 40 mg. per day in the second four days of life—20 to 30 mg. per kilo weight during the first four days, 8 to 10 mg. per kilo the second four days of life. Uric acid nitrogen made up from 18 to 20 per cent. of the total nitrogen during the first three days of life. Schloss and Crawford seemed to think that the greater excretion of uric acid in the late ligation cases points to the cellular elements of the blood as the origin of this uric acid. This theory is strengthened, perhaps, by the fact that in a case of Schwarz's[45] the uric acid in the urine was greatly increased in a baby 11 days old immediately after a transfusion, being 25 per cent. of the total nitrogen.

CREATININ AND CREATIN

The excretion of creatinin and creatin in the urine is still under considerable discussion. Whether one is derived from the other or not, or just where the creatin is changed to creatinin, is unknown. In the adult, creatinin is constantly present in normal urines and creatin is rarely if ever present. During febrile states, or in cases of fasting or in negative nitrogen balance, creatinin may be increased in urine, and creatin may be present in varying quantities, even greater than creatinin.[25] Creatin is normally found in the muscles, which are supposed to be the depot for the body. Creatinin, however, is not found in muscles. The ingestion of creatin does not increase the excretion of creatinin in the urine (Folin[46]). The protein intake does not affect the amount of creatinin in the urine and this excretion is remarkably constant in normal individuals under similar conditions. (Folin, Hoogenhuyze and Verploegh;[47] Wolff and Shaffer[48] and Shaffer.[49]) Folin believes that the creatinin nitrogen co-efficient is an indicator of endogenous nitrogen metabolism, while Shaffer more specifically thinks it is an expression of the endogenous muscular metabolism. Folin

45. Schwarz and Ottenberg: Am. Jour. Med. Sc., July, 1910.
46. Folin: Jour. Biol. Chem., Am. Jour. Physiol., 1905.
47. Folin, Hoogenhuyze and Verploegh: Ztschr. f. Physiol., xxiii, 1.
48. Wolf and Schaffer: Jour. Biol. Chem., 1908, p. 439.
49. Schaffer: Am. Jour. Physiol., xxii, 445.

further showed that the amount of creatinin excreted depended on the weight of the subject and more explicitly on the amount of muscular weight, or, as Shaffer puts it, "active protoplasmic tissues." In the adult Folin found the creatinin excretion to be 20 to 24 mg. per kilo body weight and Shaffer 18 to 30 mg. per kilo. In a boy of 5 Schwarz found 6.1 to 7.7 mg. per kilo weight—150 to 160 mg. in twenty-four hours. Amberg and Merrell[33] found 26 to 39 mg. excreted in the urine of infants, or 6.7 to 9.9 mg. creatin nitrogen per kilo body weight. These were children beyond the period of physiologic loss. It is especially interesting to note the figures for the first few days of life. This Sedgwick[50] has done in seven cases during the first few days of life. It varied considerably with the amount of urine excreted and as the weight is not included in his table it is impossible to reckon the creatinin co-efficient. The excretion was up to 25 mg. creatinin in twenty-four hours. Sedgwick was further able to demonstrate the presence of creatinin in the amniotic fluid.

AMINO-ACIDS

Embden and Reese[51] and Plaut and Reese[52] found glycocoll in normal urine and only faint traces of other amino-acids. Abderhalden and Schittenhelm,[53] on the other hand, did not find them in the urine unless there was a disturbance in the protein metabolism. Samuely[54] found glycocoll in the normal urine of two new-born infants. Langstein and Reitschel[55] did not find any amino-acids in normal urine. Von Reuss[56] found glycocoll in the urine of infants without relation to age or food. Schultz,[57] using Sorenson's method modified by Frey and Gigon, examined the urine of infants on the breast and on cow's milk, and found 8.5 per cent. amino-acid nitrogen to total nitrogen in the former and 6.7 per cent. amino-acid nitrogen in the latter. These

50. Sedgwick: Creatinin Metabolism, Jour. Am. Med. Assn., 1910, lv, 1178.
51. Embden and Reese: Beitr. z. chem. Phys. u. Path. (Hofmeister), vii, 441.
52. Plaut and Reese: Beitr. z. chem. Phys. u. Path. (Hofmeister), vii, 425.
53. Abderhalden and Schittenhelm: Ztschr. f. phys. Chemie, xlvii, 343.
54. Samuely: Ztschr. f. phys. Chemie, xlvii, 376.
55. Langstein and Reitschel: Biochem Ztschr., i, 75.
56. Von Reuss: Wien. klin. Wchnschr., 1909, p. 158.
57. Schultz: Jahrb. f. Kinderh., 1910, lxxii.

figures are fairly constant for the same child but vary greatly in different children, both in health and disease. In cases of children very much under weight from alimentary disturbances but well at the time of examination, the amino-acid nitrogen in the urine was from 6.7 to 8.5 per cent. In cases of dyspepsia ("Bilanzstörung" of Finkelstein) the amino-acid nitrogen was from 8.5 to 10 per cent.

50 East Ninety-First Street.

THE RÔLE OF MINERAL SALTS IN THE METABOLISM OF INFANTS *

B. RAYMOND HOOBLER, M.D.
NEW YORK

It is the purpose of this paper to present, in rather broad outlines, the part which mineral salts play in carrying on the physiologic functions of the body, and in what manner they contribute to the various pathologic processes to which the infant and young child are subjected.

This field of metabolic research has been the last to be undertaken, and just now we are coming to realize its vast importance, not only in connection with their own functions, but in connection with the influence they have on the metabolism of fat, protein and carbohydrate. The chief reason for having failed to realize the importance of the mineral salts in metabolism is that it has long been thought that the salts contributed in no way to the nourishment of the child. It has been only recently that they have taken their rightful place as indirect energy producers.

HISTORICAL

The first investigator to concern himself with the value of mineral salts was von Liebig,[1] who, as early as 1840, studied the action of mineral salts both in animal and vegetable life, and many of his early deductions have become firmly fixed as laws in the field of mineral salts metabolism. C. Voit[2] is another investigator whose work on the action of sodium chlorid, as early as 1860, first gave to that salt its prominence above all others in the human economy. Vierordt was also an indefatigable worker, and as early as 1877, from meager data then present, had calculated absolute and relative heat and estimated child's metabolism. J. Forster,[3] in 1873, added his convincing experiments on the necessity of the mineral salts to the continuance of life, and these were further reinforced by the

*From the laboratories of the Presbyterian Hospital and Cornell University Medical College.

1. Von Liebig, J.: Chemie in ihrer Anwendung auf Agrikultur und Physiologie, 1876, p. 332.

2. Voit, C.: Ueber den Einfluss des Kochsalzes auf den Stoffwechsel, München, 1860.

3. Forster, J.: Ztschr. f. Biol., 1873, ix.

work of Lunin[4] in 1881. As time advanced, the roster of those who worked in the field of mineral metabolism contains the names of many notable investigators, as G. v. Bunge, Michel, Keller, Loeb, Muller, Schlossman, Blauberg, Rubner, Huebner, Freund, v. Noorden, and in these latter days the work is being carried on enthusiastically by L. Langstein, L. F. Meyer, E. Schloss, J. A. Schabad and others abroad, and by Howland, Schwartz, Talbot, Veeder, and others in this country.

A GENERAL VIEW

In undertaking a problem of this kind, it is well at the beginning to take a general view, first of the physiologic action of the mineral salts as a whole, and then to study what has been definitely determined as to the action and influence of each of the mineral constituents. Then by inquiring into the mineral constituents of the new-born and of older children, one will be in position to learn the mineral needs of the growing organism, and, knowing them, to ascertain how best to supply them, and to study the factors which enter into the proper utilization of the salts ingested in the food and to determine whether or not this utilization is sufficient to meet the demands of the growing infant.

First, then, a general view of the physiologic action of the mineral salts as a whole. Physiologists are generally agreed, and their findings confirmed by physiologic chemists, that the important functions of the mineral salts are as follows:

1. They maintain the osmotic pressure in tissue cells, blood, and body fluids; controlling the flow of water to and from tissues; any deviation from normal causing a shrinking or swelling of tissue cells.

2. They regulate the reaction of the blood and tissue fluids. A deviation from this reaction inhibits the action of the various ferments, delays chemical processes, and if such reaction suffers much variation, death results.

3. Their presence in tissues and fluids gives rise to irritability of muscle and excitability of nerve through the action of their respective *ions*. Through this function the rhythmical contractions of the heart are maintained.

4. They act as catalysts for a large series of chemical reactions which take place during the processes of absorption, retention, utilization, and form combinations with waste products of metabolism in order to effect their elimination; for example, they act as carriers of excess acid materials in oxidation processes.

5. They share in the upbuilding and growth of the body, since they are a constituent of every cell; particularly do they take part in the changes which go on in the albumin bodies as they become intimately bound with the body proteins.

4. Lunin, N.: Ztschr. f. physiol. Chem., 1881, v.

6. Their function in the intermediary metabolism of the ductless glands is very apparent from the large quantities of mineral salts found in these glandular organs.

7. Through a most excellent self-regulation, they protect against the acid poisons which the body is constantly producing.

8. Through the work of the various *ions*, electrically charged, some positively, some negatively, many important functions are being assigned to them, such as controlling body-weight, temperature, regulating the pulse, increasing leukocytes, etc. These and many more functions, not clearly defined, depend on the presence of the mineral salts in the body, and not on their presence alone, but their presence in definite relationships to one another.

ABSOLUTE NECESSITY OF SALTS

While physiologists have been busy defining the various functions of salts, other investigators have determined the absolute necessity to the maintenance of life of a certain quantity of mineral salts, and not only a certain quantity, but they have found that these salts must be in certain organic combination, as the following experiments will show:

Forster,[3] in 1873, fed pigeons on approximately ash-free diet, and found their bones brittle, and they all died within a month. He also fed dogs on salt-poor diet, and they lived from twenty-six to thirty-six days.

Lunin[4] showed by his classic experiment that the salts must be in organic combination to be available. He found that mice thrived well on dried whole milk, but that if the salts were extracted from the milk, and they were fed only the protein, fat and carbohydrate, they shortly died, and further, after abstracting the salts, if he substituted the same quantity of other mineral salts, adding them to the protein, fat and carbohydrate, the mice died. Furthermore, mice fed on ash-free food, plus sufficient sodium carbonate to take the place of the usual salts, lived twice as long as mice fed only on ash-free diet; nevertheless, they succumbed, demonstrating that even with the necessary amount of bases carbonates cannot supply the salt needed.

Rohmann[5] added further confirmation to the value of salts. He fed mice a mixture of simple organic and inorganic food-stuffs. These mice lived and were able to produce young, but the latter could not be raised on artificial food, nor could they be made to produce living young.

It is evident from this latter experiment that artificial foods may be sufficient for the adult, whose supply of minerals is well established, but it is not sufficient to produce healthy offspring.

Abderhalden[6] believes that the same physiologic importance of salts exists for the animal kingdom as has been shown by von Liebig and others to exist for the vegetable kingdom.

---

5. Rohmann: Klin.-therap. Wchnschr., 1902, No. 40.

6. Abderhalden: Physiological Chemistry, p. 356.

The salts have a very important bearing on the absorption and retention of other food constituents, e. g., in a large nitrogen retention there is usually a large ash retention, and when ash is eliminated in large quantities there is usually an accompanying loss of nitrogen.

T. B. Robertson[7] points out how intimately the precipitation and coagulation of protein depends on the salts present in the solution as *ions*. Indeed it is becoming more and more to be appreciated that the various food constituents have a very intimate influence, the one on the other, and it is along this particular line that metabolism studies are directing themselves.

Recognizing, then, that the mineral salts are necessary to life, let us inquire what salts, and in what proportion in the body, Nature has stored them, by the action of which not only life is maintained, but energy developed and growth permitted. We are indebted to a number of investigators for information on the ash-content of the human organism both during fetal life and later.

Fehling[8] gives us the following figures of the ash-content at different periods of fetal life:

Period of Life.	Ash Content; Per Cent. of Total Weight.
Fetus, 6 weeks	.001
Fetus, 4 months	.98
Fetus, 5th month, first half	1.4
Fetus, 5th month, second half	1.43
Fetus, 6th month	1.94
Fetus, 7th month	2.94
Fetus, 8th month	2.82
Fetus, 9th month	3.3
In the new-born	2.7
In the adult	4.4

It will be noted, therefore, that from the earliest observation of fetal life to those on adult bodies, there is a gradual increase of the ash-content. This increase is most rapid in terms of percentage of body weight during the fetal period, and thereafter the increase is much slower.

Let us now ask ourselves the question as to the mineral constituents contained in the total ash-content and study their relative amounts. Hugounencq[9] has given us this information for fetal life, and Soldner[10] for the new-born. Soldner found that there was 75 gm. of ash in a new-

7. Robertson, T. B.: Jour. Biol. Chem., May, 1911.
8. Fehling: Cited by Freund, in Pfaundler and Schlossman, i, 363.
9. Hugounencq: Compt. rend. Soc. de biol., li, 537.
10. Camerer and Soldner: Ztschr. f. Biol., 1900-3, xxxix, xl, xliii, and xliv.

born child which was equal to 2.7 per cent. of its body weight, or 9.4 per cent. of the dry residue.

	Total Ash in Parts Per 100							
Period of Life.	Cl	P_2O_5	SO_3	CaO	MgO	K_2O	Na_2O	Fe_2O_3
Fetus, 5 months.....	8.59	34.36	1.8	32.5	1.58	8.28	12.62	.4
Fetus, 6 months.....	7.75	34.94	1.78	34.6	....	7.21	10.62	.39
Fetus, 7 months.....	8.53	35.39	1.46	34.13	1.17	8.45	10.95	.398
New-born (Soldner), average of 6.....	6.61	.....	2.02	38.08	1.43	7.06	7.67	.83

Soldner, arguing from the average ash content of six new-born infants, concluded that there was a daily need of 1.4 gm. of mineral ash, and an infant should retain of the intake, chlorin 14 per cent., potassium 11 per cent., sodium 35 per cent., CaO, MgO and P_2O_5 at least 65 per cent. of the intake.

It will be noted that phosphorus and calcium make up considerably over half; sodium about an eighth, and potassium and chlorin about a twelfth of the total ash-content, and that sulphur, magnesium and iron make up but a small part of the total.

Bunge,[11] after a careful study of the mineral contents of the milk of lower animals and estimating the daily requirements of their offspring, attempted to show that the ash-content of the body was in correct proportion to the ash-content of the various animals. But when this was applied to the nursing infant his analogy failed, and the problem did not solve itself as readily as this hypothesis would indicate. It is evident that the main metallic elements are calcium, sodium, potassium and magnesium; the main acid salts being phosphoric, hydrochloric, carbonic and sulphuric, calcium phosphate being the most abundant of all the salts.

It should be further noted that the phosphorus and calcium content of the body increases in percentage, and that the other elements remain at the same or less percentage, but of course their absolute amount gradually increases.

The difference between the ash-content of a new-born and the ash-content of a 4-months' old child represents the change which must take place in the mineral salt storing. In actual figures the child must add to his weight, during the first four months, the following quantities of the various minerals:

11. Bunge: Cited by Freund, Pfaundler and Schlossman, Vol. i.

	Gm.
K_2O	2.0
Na_2O	2.57
CaO	11.75
MgO	.31
Fe_2O_3	....
P_2O_5	10.48
Cl	1.12
S	....

It will be noted what really small quantities of the mineral salts are added to the body—extremely small when we consider the large quantity which a child during the first year must ingest. It is estimated that only about 4 per cent. of intake goes to growth in early months and later only half that amount. It is evident that a large quantity must be worked over. Taking mother's milk as a basis, during the first twelve months of life there is approximately 800 gm. of total ash ingested. This is divided among the various mineral salts as follows:

	Gm.
K_2O	276.
Na_2O	19.6
CaO	157.6
MgO	27.2
Fe_2O_3	8.0
P_2O_5	117.6
Cl	117.6
SO_3	57.4
Total	791.0

If we take cow's milk as a basis, the picture is entirely different. Taking the average amount fed as outlined in Dr. Holt's text-book, an infant would ingest approximately 1,500 gm. of total ash during the first year of life, which would be divided among the various mineral constituents as follows:

	Gm.
K_2O	377.0
Na_2O	93.0
CaO	344.0
MgO	41.0
Fe_2O_3	4.2
P_2O_5	487.4
Cl	84.0
S	69.4
Total	1,500.0

This naturally leads us to a two-fold conception of the use which the body makes of the salts. First, a certain small per cent. is firmly bound with the tissues of the body and only escapes when such tissues are

destroyed in oxidation; and a second group which are simply held in solution in the body fluids ready to be excreted, or to act as bases or alkalies to take up the products of cell destruction, or combine with acids set free in the processes of catabolism, or in the form of *ions* to subserve definite physiologic functions. It should be borne in mind that only a small part of the mineral salt intake in any day's feeding is added as an integral part of the tissue, and that by far the largest part is simply held in solution awaiting its excretion, either through the skin, urine or back into the intestinal canal. With sulphur and phosphorus the problem is a little more complicated, as these two substances are in exceedingly close chemical relationship with albumin, and before they can be set free the foreign albumin molecule must be torn down before it can be again rebuilded into the tissue substance and fluids of the host.

Having noted just what minerals and acids are present in the body at the end of fetal life, it behooves us to inquire into the method by which we can continue to supply the needs of the infant as relates to its mineral constituents so as best to foster its normal growth and aid in supplying its daily energy requirement. Nature has supplied us with a most excellent criterion by which we may reach a solution of this problem, viz., in normal mother's milk. Let us, therefore, address ourselves to a study of Nature's method of supplying the need of the growing infant by carefully considering the mineral constituents and their relative proportions in mother's milk.

In early mother's milk, i. e., colostrum, according to Camerer,[12] we have a marked increase from the first to the seventh day in the ash-content as follows:

Day after delivery	1	2	3	4	5	6	7
Ash content in per cents	0.1	0.5	0.7	0.9	1.0	1.1	1.3

Thus Nature provides in the early nursing period for a very rapid increase in the mineral constituents of the food. In mother's milk there is about 2.0 gm. of total ash to 1,000 gm. of milk. This 2 gm. of ash is divided among the various mineral constituents according to various authors, as follows:

12. Camerer: Cited by Freund in Pfaundler and Schlossman, i, 386.

In 1,000 gm. of mother's milk, there is, according to

	Bunge 1[15]	Bunge 2[15]	Camerer[13] and Soldner	Blauberg[14]
	Gm.	Gm.		Gm.
K_2O	0.780	0.703	0.884	0.69
Na_2O	0.232	0.257	0.357	0.049
CaO	0.328	0.343	0.378	0.394
MgO	0.064	0.065	0.053	0.068
Fe_2O_3	0.004	0.006	0.002	0.02
P_2O_5	0.473	0.469	0.310	0.294
Cl	0.438	0.445	0.591	0.294
SO_3	....	.....	.....	0.143

The ash-content of mother's milk does not remain constant, as is shown by Soldner[16] in his examinations of mother's milk on the eighth and seventieth days. In 1,000 gm. of mother's milk on the eighth day, there was 3 gm. of total ash, and in the same quantity on the seventieth day there was 2 gm. of total ash divided as follows:

	Eighth day	Seventieth day
	Gm.	Gm.
K_2O	1.008	.259
Na_2O	.448	.176
CaO	.376	.381
MgO	.054	.052
Fe_2O_3	.0022	.00125
P_2O_5	.320	.288
SO_3	.096	.063
Cl	.716	.342

From the above, it would seem that the fixed alkalies K and Na diminish greatly as does also the chlorin content of the milk, while the bone-forming constituents, viz., calcium, phosphorus and magnesium, remain nearly constant. In cow's milk the relations are entirely different as is shown by the exceedingly large ash-content of 7.8 gm. per 1,000 gm. of milk as against 2 gm. in 1,000 gm. of mother's milk. Not only does cow's milk contain more ash, but in vastly different proportion of mineral constituents than mother's milk, as will be seen by the following table when compared with the preceding table showing mineral contents of the ash of mother's milk. In 1,000 gm. of cow's milk there is:

13. Camerer and Soldner: Cited by Albu-Neuberg, Mineralstoffwechsel, p. 51.

14. Blauberg: Cited by Langstein and Meyer Säuglingsernährung und Säuglingsstoffwechsel, Wiesbaden, 1910, page 15.

15. Bunge: Cited by Albu-Neuberg, Mineralstoffwechsel, p. 51.

16. Soldner: Cited by Freund, in Pfaundler and Schlossman, p. 377.

	Bunge[15] Gm.	Soldner[13] Gm.	Hoobler Gm.	Soldner[17] Gm.
K_2O	1.766	1.720	.....	1.885
Na_2O	1.110	0.51	.....	0.465
CaO	1.599	1.980	1.600	1.72
MgO	0.210	0.20	0.167	0.205
Fe_2O_3	0.004	.....	.....	0.021
P_2O_5	1.974	1.82	2.140	2.437
Cl	1.697	0.98	1.86 (NaCl)	0.820
S	....	.....	0.33638	....

It will be seen that in the same quantities of milk, that of the cow contains over twice as much potassium, five times as much sodium, phosphorus and calcium, four times as much magnesium and chlorin and six times as much sulphur. And, further, these salts are not in the same organic combination in one as in the other, as shown by Keller,[18] and also by Schlossman,[19] as relates to phosphorus, and when we consider that it is the organically bound salts only, as shown by Lunin,[4] which are available, this factor is a very important one.

Not only are the salts organically bound, but there is a peculiar specificity about the whey containing the salts of mother's milk. Meyer[20] has shown that not only the protein and fat of mother's milk, but even the casein and fat of cow's milk, are well absorbed and retained when mixed with the whey of mother's milk. Children fed on the fat and protein of mother's milk mixed with the whey of cow's milk are not able to utilize these food products and do badly. It would seem that some constituent in mother's milk whey contains the essential dynamic force for making the casein and fat of both mother's and cow's milk available for nutritive purposes.

Having now considered separately the salts of the child's body and the salts of the two most common foods, let us study the processes which take place when these foods are ingested by the infant. It would contribute to a continuity of thought if we were to follow each individual salt through its various metabolic steps under perfectly normal conditions and discuss them under the heads of ingestion, absorption, retention and elimination, considering the results obtained by investigators in the use of mother's milk and cow's milk.

---

17. Soldner: Cited by Langstein and Meyer, Säuglingsernährung und Säuglingsstoffwechsel, Wiesbaden, 1910, page 15.

18. Keller, A.: Arch. f. Kinderh., 1900, xxix.

19. Schlossman: Arch. f. Kinderh., 1905, xl.

20. Meyer, L. F.: Cited by Meara, Problems of Nutrition in Early Life, Arch. Pediat., xxvii, 401.

TOTAL ASH

Food	Intake	Elimination		Absorption			Retention		
		Feces	Urine	Gm.	Percent.	Per Kilo	Gm.	Percent. of Intake	Per Kilo
Mother's milk (Blauberg)	1.13	0.193	0.373	0.937	82.9	....	0.56	49.5	....
Mother's milk (Blauberg)	1.32	0.24	0.47	1.08	81.8	....	0.61	45.9	....
Cow's milk (Soldner)	6.841	2.686	3.1341	4.15	60.7	....	1.013	14.8	....
Diluted cow's milk, 2.1% fat (Hoobler)	8.9691	4.2651	4.7966	4.7039	53.0	.565	.....	....	....
Cow's milk, 4% fat (Hoobler)	9.4808	3.1390	3.0834	6.3418	66.8	.808	2.8917	43.5	.368
Cow's milk and cream, 5.4% fat (Hoobler)	8.7634	1.8675	4.1493	6.8959	78.6	.861	2.7465	37.8	.344
Cow's milk (Blauberg)	6.84	2.68	3.13	4.15	60.7	....	1.01	14.8	....

Figures given above are in grams in 24 hours.

After having considered these steps in normal metabolism, I shall address myself briefly to abnormal conditions of metabolism, desiring rather to give most attention to the consideration of the normal. I shall take occasion to consider, along with the findings of literature, some results obtained by me in a series of metabolism studies which I have carried out in the wards and laboratory of the Presbyterian Hospital on a perfectly healthy infant of 9 months who had been fed on cow's milk from the time of his birth, details of the experiment, as relates to nitrogen metabolism, having already been published.[22]

TOTAL ASH

I will first consider the figures covering the entire mineral metabolism as represented by total ash, and will then discuss its various phases.

INGESTION

First let us consider the intake. It should be remembered that mother's milk is relatively poor in ash-content while that of cow's milk is exceedingly rich, so that one is not surprised to note that the intake of total ash through breast feeding is very much less than with cow's milk feeding. From the figures of Blauberg, Soldner, and my own determinations, the ash intake in artificially fed children is from six to nine times greater than that of breast-fed children.

ABSORPTION OF TOTAL ASH

Various observers have recorded their findings of ash absorption in mother's milk, varying from 81.82 per cent. by Blauberg to 53 per cent. of intake by Schlossman; Biedert's determination was 77 per cent., and that of Rubner and Heubner 79.42 per cent., while the absorption of total ash of cow's milk by different authors is as follows (see also p. 52):

	Per cent.		Per cent.
Soldner	60.7	Biedert	65.1
Schlossman	70.	Hoobler	53.
Tangl	62.1	Hoobler	66.8
Blauberg	53.72	Hoobler	78.6

It will be seen that the absorption per cent. is 15 per cent. to 25 per cent. better on mother's milk, but because of the large intake the actual amount absorbed is very much larger in cow's milk feedings than in breast-fed. For example, 1.08 gm. was absorbed in twenty-four hours on

22. Hoobler: Arch. Pediat., 1910, xxvii, 853.

mother's milk, while on cow's milk from 4 to 6 gm. were absorbed daily. Thus approximately four to six times more is absorbed in artificial feeding.

As we shall see later, this better absorption of mother's milk ash lies in the fact that calcium, magnesium and phosphorus are much better absorbed. As was demonstrated in my work on the various fat feedings, and now being published in the Presbyterian Hospital Report of this year, nitrogen, chlorin, sulphur and magnesium were absorbed in the same ratio as these elements existed in the food. The greatest variations from the ratio in the food occurred in calcium and phosphorus.

RETENTION

Without doubt the best criterion of availability and utilization of any given food-stuff is not its large per cent. of absorption, or even its large absolute amount of absorption; but rather the absolute amount retained. Literature does not yet contain reports which cover sufficient periods of investigation to feel quite sure that these so-called absolute retentions are permanent or simply transitory, since it takes weeks to utilize and eliminate the mineral salts. Therefore a prescribed diet should be carried out for weeks instead of days for most accurate results. However, the reports in literature show that the ash of mother's milk is well retained and this is but natural, for the salts come to the infant in much better form for utilization than in cow's milk.

In Blauberg's case on mother's milk (see total ash tabulation), the absolute retention was 0.61 gm., being 45.9 per cent. of the intake. In cow's milk feeding, the per cent. of retention is lower but the absolute amount is higher, owing to the much richer ash-content of the cow's milk. Blauberg's case on cow's milk feeding, having a retention of 14.8 per cent. of intake, represented an absolute amount of 1.013, being nearly twice the amount retained under mother's milk feeding. In my 9-month child there was retained 2.89 gm. or 43.5 per cent. intake. Blauberg found that with mother's milk feeding all the minerals were retained with the exception of sodium; in cow's milk there was a loss in Cl, S, and Na. It would seem that each child is a law unto itself so far as retention of mineral ash is concerned. It apparently takes it on just in accordance with the demands of physiologic growth.

In my determinations in connection with various strengths of fat in foods, I found that as compared with nitrogen retention, the retention of the mineral salts was relatively poorer. This poor retention was most

marked on the lower fat food, better on the medium fat diet, and best as regards the absolute amount retained on the high (5.4 per cent.) fat diet. Retention of the salts in proportion to nitrogen was never in the same proportion as existed between the salts and nitrogen of the food.

ELIMINATION

The elimination through the feces and urine differs in amounts on mother's and cow's milk. In mother's milk feeding, one-third of the salts are eliminated through the feces and two-thirds through the urine, while in cow's milk feeding about half is eliminated by the urine and half by the feces, though the figures of different investigators vary. In my own figures the ash of the feces was three times as large on a 2.1 per cent. fat mixture as on a 5.4 per cent. mixture.

THE ANOMALIES IN THE METABOLISM OF TOTAL ASH

In the elaboration of Finkelstein's theory of food disturbances in infants and children, L. F. Meyer[23] has attributed to the mineral salts certain deleterious influences.

In each of Finkelstein's four stages of nutritional disturbance, Meyer finds that there is some anomaly in the salt metabolism. In the stage of *"Bilanzstörung,"* there is decreased retention of the alkaline earths. There is also a lessened retention of other salts.

In the stage of dyspepsia, the salt elimination by the feces is increased but the ash balance is not markedly changed. In the stage of decomposition the entire picture is determined by the loss of the mineral salts, particularly through the loss of the fixed alkalies. Through the fatty acids in the stools, the Ca and Mg are used up. The diarrheal stools of this period are due largely to alkali loss. The condition of relative acidosis of Steinits (and of alkalipenia of Pfaundler) takes place during this stage, due to the loss of alkali.

In the fourth stage, of intoxication, the salt metabolism is little known. There is a negative balance of chlorin and probably of the other mineral constituents. Whether the salt loss controls the water loss or vice versa is still a question, but since the urine is much decreased and the output of water by the feces is increased, it would seem that the salts were accountable for this diversion of the water elimination. It is evident that salts play an important part in every digestive disturbance of the infant and young child.

---

23. Langstein and Meyer: Säuglingsernährung und Säuglingsstoffwechsel. Wiesbaden, 1910, pp. 111-166.

CALCIUM

The calcium need of the growing infant is well met through the abundance of its salts in the milk, either of mother's or of cow's. Calcium makes up one-fifth of the ash of mother's as well as of the ash of cow's milk. Calcium is taken into the body in organic and inorganic form. The organic combination is present in milk, yolk of eggs and vegetables, and the inorganic form in water used as a diluent and for drinking.

The importance of the calcium salts in the developing organism can hardly be overestimated. Physiologists[24] have shown that the calcium *ions* in the blood, though in small quantity, are yet absolutely necessary to the irritability of muscle. If calcium is present in too large quantities, as compared with Na and K *ions,* there is produced a tonic contraction known as calcium rigor.

Calcium has a definite specific action of its own and cannot be replaced by other earthy bases, as magnesium and strontium, as stated by Stewart.[25] The fact is well known that calcium is necessary to ferment action as shown by the coagulation of blood and the precipitation of casein in milk. Calcium is much the largest mineral constituent of the body. Its most common salt is calcium phosphate, which makes up a large part of the bone salts.

Jacques Loeb[26] has shown the necessity of calcium salts for the development of the lower forms of life, and Blauberg has shown that children who cannot metabolize calcium cannot survive.

Mother's milk contains only about 20 per cent. as much calcium as cow's milk; therefore we would expect a considerable variation in its absorption and retention, as is shown by the following:

CALCIUM AS CaO

The calcium of mother's milk is 0.394 grams in 1,000 gm. I found calcium of cow's milk to be 1.6 grams in 1,000 gm., or nearly four times as much in cow's as in mother's milk. (See also tabulation page 15.)

It will be noted first that the calcium intake in cow's milk feeding is about eight times greater than in mother's milk; that the amount actually absorbed and retained is four times greater on cow's milk than on mother's milk. However, a much larger percentage of mother's milk calcium is retained. It is evident, therefore, that the calcium of mother's

24. Howell: Physiology, Ed. 2, 1907.

25. Stewart: Physiology, Ed. 1910, p. 542.

26. Loeb, J.: Cited by Meyer, Jahrb. f. Kinderh., lxxi, 1.

milk is much better metabolized than the calcium of cow's milk, and since a healthy nursing infant shows no signs of a deficiency of calcium, we may well consider the amount which it gets as being the true calcium need. The absorption of calcium depends in part on the presence of accompanying salts; for example, if much alkali bases are present in the intake the absorption is diminished, whereas NaCl assists in calcium absorption. Calcium is more readily absorbed on flesh than on a vegetable diet.

ELIMINATION

It should be noted that the elimination of calcium is almost entirely through the feces; only 5 to 10 per cent. of the intake appears in the urine. This does not mean that the calcium is not well absorbed, but that it is excreted into the large intestine, as is proved by the fact that larger quantities of calcium are found in the large intestine than in the small intestine. It was Voit[27] who showed that 0.15 gm. of calcium per day was excreted from the inner surface of the intestine.

The amount of calcium excreted in the urine of infants fed on breast and cow's milk does not vary greatly, but the amount which appears in the feces varies greatly, being in some instances twenty times greater. Calcium makes up a quarter or a third part of the dried feces of cow's-milk-fed children, as against a much smaller portion in breast-fed. The form in which the calcium usually appears in the feces is that of the insoluble soaps, or in the form of calcium phosphate.

In my series of studies the elimination of calcium in the feces was greater on milk of lower fat content. As fat was increased in the food, the calcium was diminished in the feces. The calcium eliminated in the urine appears along with magnesium, bound with phosphoric, carbonic and uric acids. Iron is another mineral constituent which is excreted very poorly through the urine, and this leads one to group these two constituents together and to inquire if there are other characteristics. It should be noted that their presence in many organs, for example the thyroid gland, the liver, the spleen and the ovaries, suggests physiologic and chemical affinities as pointed out by Albu and Neuberg.[28] The internal secretions which play such a part in intermediary metabolism of the mineral salts, may be largely affected by the relationship of these two minerals. Calcium and phosphorus are closely allied in the bones, in the ovaries, and in the thyroid gland.

---

27. Voit: Cited by Howell, Physiology, Ed. 2, p. 834.
28. Albu-Neuberg: Mineralstoffwechsel, Berlin, 1906, p. 70.

CALCIUM AS CaO

Food	Intake	Elimination		Absorption			Retention		
		Feces	Urine	Gm.	Percent.	Per Kilo	Gm.	Percent.	Per Kilo
Mother's milk (Blauberg)	0.2884	0.0952	0.0127	.....	....	....	0.176	62.4	....
Mother's milk (Blauberg 5 mos.)	0.2720	0.0660	0.0310	0.2060	75.8	....	0.175	64.5	.026
Cow's milk (R. & H. 7½)	2.0824	1.142	0.0166	0.9370	45.1	....	0.924	44.4	.122
Diluted cow's, 2.1% fat (Hoobler)	2.0536	2.2687	0.0301	Negative	....	....	Negative	....	....
Cow's whole milk, 4% fat	2.0500	1.6962	0.305	0.3538	17.2	.045	0.3233	15.7	.041
Cow's milk and cream, 5.4% fat	2.0923	0.9515	0.0085	1.1408	54.5	.142	1.1322	54.1	.142

Figures given above are in grams in 24 hours.

THE ANOMALIES OF CALCIUM METABOLISM

As a rule there is a great individual difference in the amount of calcium absorbed, and a further difference in the ability to retain the calcium absorbed. Rarely is such a condition due to the lack of calcium in the food, although many artificial foods are very poor in calcium. A diet containing less than 1 to 1.5 gm. CaO daily should be considered calcium-poor, except when on mother's milk feeding.

It has been shown that when calcium is purposely withheld from the diet of young puppies, rachitis develops, and the bones of young pigeons fed on calcium-poor diet are very fragile (Forster[3]). In the bones, in rachitis the mineral constituents are depleted, particularly calcium and phosphorus. The total ash of bones which normally is 65 per cent. falls to as low as 25 per cent. and the main loss falls on the calcium phosphate. The calcium loss in rachitis is largely through the intestine, with but little change in urinary calcium. In feces of rachitis, there is an increased elimination over that of healthy children, as shown by J. A. Schabad.[29] In rachitis particularly the weak point in the metabolism cycle may be the inability of the bones themselves to take up and build into bony tissue the calcium and phosphorus brought to them by the fluids, as has been pointed out by Albu and Neuberg.[28] The fact that calcium has much to do with the function of the nervous system has been shown by the calcium disturbances in tetany, as demonstrated by Schabad.[30] Further, the large proportional content of the brain tissue of the new-born in calcium (0.168 per cent. CaO), as compared with an 8-year-old child's brain (0.05 per cent.) speaks further confirmation of this. There is a very appreciable loss of calcium from the nerve structures during the first year of life. Quest[31] found less calcium in the brains of children who died of tetany than of children of the same age without tetany.

Schloss[32] has more recently shown that subnormal body temperature in some cases depends on the presence of calcium *ions*. In the symptom-complex which Finkelstein calls *Ernährungstörung,* during the stage of *Bilanzstörung,* Meyer[23] has shown that there is a decreased retention of calcium due in part to the fact that the fats of the stools are increased, and these demand the alkaline earth to neutralize the fatty acids. There

29. Schabad, J. A.: Arch. f. Kinderh., liii, 241.

30. Schabad, J. A.: Monatschr. f. Kinderh., ix, No. 1; Jahrb. f. Kinderh., l, No. 1.

31. Quest: Cited by Freund, in Pfaundler and Schlossman, i, p. 285.

32. Schloss: Cited by Langstein and Meyer, Säuglingsernährung und Säuglingsstoffwechsel, Wiesbaden, 1910, p. 21.

may be such a demand that not only will no calcium and magnesium be retained, but there may be an actual withdrawal of these salts from the body. This may account for a portion of the loss of weight in this stage of food disturbance.

IRON

Cow's milk and mother's milk contain about the same amounts of iron. Each is very poor in iron, and were it not for the relatively large amount stored in the liver and blood of the new-born there would be a deficiency in the early months of feeding. The following table shows that the form in which the iron is present has a large bearing on its availability. The iron of goat's milk is poorly absorbed and poorly retained, while the iron of mother's milk is well absorbed and well retained. Iron is eliminated almost entirely through the feces but a very small quantity through the urine.

Iron plays an important part in metabolism. It is specially important in the formation of the hemoglobin molecule. It acts as a catalyst in oxidation processes, especially in the group of nucleoproteins, as has been shown by Spitzer[44] and by Manchot.[45] Iron is presented for consumption in both the organic and inorganic form. The organic forms occur in the nucleoalbumins, in milk, yolk of eggs and in many vegetables.

IRON AS Fe_2O_3

In 1,000 gm. mother's milk, .02 gm. to .04 gm.
In 1,000 gm. cow's milk, .021 gm. (Abderhalden).

		Elimination		Absorption		Retention	
Food	Intake	Feces	Urine	Gm.	%	Gm.	%
Mother's milk	.00705	.00084	.00055	.00621	88.09	.00566	82.28
Goats' milk	.00344	.00259	.00009	.00085	24.71	.00076	22.09

Figures given above are in grams in 24 hours.

MAGNESIUM

Magnesium and calcium are very closely connected in the metabolic function. They occur in the organism in much the same places and as salts of the same acids. Their proportion is CaO:MgO::40:1. Magnesium has a little wider distribution in the body tissues than does calcium. The latter occurs almost entirely—at least 99 per cent.—in the bones, while magnesium is found in muscle-tissue as high as 0.04 per cent. The part which magnesium plays in bone structure is important. Magnesium

44. Spitzer: Cited by Albu and Neuberg, Mineralstoffwechsel, Berlin, 1906, p. 151.

45. Manchot: Cited by Albu and Neuberg, Mineralstoffwechsel, p. 151.

Magnesium as MgO

In 1,000 gm. mothers' milk there is 0.068 gm. MgO.
In 1,000 gm. cows' milk there is .205 gm. MgO.

Food	Intake	Elimination		Absorption			Retention		
		Feces	Urine	Gm.	Percent.	Per Kilo	Gm.	Percent.	Per Kilo
Mother's milk (Blauberg)	0.047	0.0157	0.014	.....	....	....	0.0175	37.2	....
Cow's milk (Soldner)	0.15017	0.0944	0.03718	.....	....	....	0.017	11.5	....
Diluted cow's milk, 2.1% fat (Hoobler)	0.10843	0.0058	0.0134	.10258	94.6	.123	0.0891	82.1	.011
Whole cow's milk, 4% fat (Hoobler)	0.07755	0.0300	0.04861	.04746	61.3	.045	Negative	....	....
Cow's milk and cream, 5.4% fat (Hoobler)	0.14999	0.0828	0.01909	.06719	44.7	.008	0.04809	32.0	.006

Figures given above are in grams in 24 hours.

makes up about 10 to 15 per cent. of the total ash of bone. The relation of magnesium in these structures is about 1:9. The magnesium table on page 123 indicates that the Mg need of the growing infant on mother's milk is 0.047. Bunge, as cited by Albu and Neuberg, gives the magnesium need as 0.6. This seems rather high, for, since there is about 0.06 gm. Mg in a litre of mother's milk, it would require 10 litres to satisfy this need. Blauberg's breast-fed infant got but 0.047 gm. daily. The intake when fed on cow's milk varied; according to Soldner the daily intake was 0.15 gm., while my determinations showed intake varying from 0.07 to 0.15.

ABSORPTION

The absorption of magnesium which takes place through the small intestine is relatively very good. My determinations gave 94.6 as the per cent. of intake which was absorbed when feedings were low in fat. As the fat content of the food was increased, there was relatively poorer absorption, the percentages being 61.3 on a 4 per cent., and 44.7 on 5.4 per cent. fat mixture.

RETENTION

The retention of magnesium in my series was better on 2.1 per cent. fat mixture than on the 5.4 per cent. mixture. This retention varied inversely with the calcium retention so far as the amount of the fat in the food is concerned. In my findings for calcium, retention was poorest on lower fat mixtures and improved on the higher fat mixtures.

ELIMINATION

Excretion occurs both through urine and feces. On mother's milk in Blauberg's case, the excretion through either channel was about the same, while in cow's milk in some instances it was higher in urine and in others it was higher in the feces. In any event, the excretion is very small and that through the urine occurs as triple phosphates.

ANOMALIES OF RETENTION

There is more or less relation between Ca and Mg in the formation of oxalic acid concretions. It has been found that if the ratio of CaO to MgO be as 1 to 0.8 the concretion may be kept in solution. The smaller the calcium and the larger the Mg content the easier becomes the solution of calcium oxalate.

PHOSPHORUS

Of all the mineral elements, perhaps none has been studied more assiduously than phosphorus. Phosphorus is brought into the body in

Phosphorus as P_2O_5

	Total Gm.	Organically Bound, Gm.
In 1,000 gm. mother's milk	.294	42.3
In 1,000 gm. cow's milk	2.437	46.
In 1,000 gm. cow's milk (Hoobler)	2.140	....

Food	Intake	Elimination		Absorption			Retention		
		Feces	Urine	Gm.	Percent.	Per Kilo	Gm.	Percent.	Per Kilo
Mother's milk	0.2768	0.0363	0.0481	.....	....	....	.192	69.13	.....
Mother's milk, 5 mos.	0.2030	0.0220	0.088	0.1810	89.1	....	.093	45.9	.0138
Cow's milk	1.4429	0.5352	0.5003	.....	....	....	.4074	30.7	.....
Cow's milk (Keller's 2¾ mo)	0.8248	0.1073	0.4106	0.7174	87.1	....	.3068	37.2	.0626
Cow's milk (Blauberg's 7½ mos.)	2.0605	0.9627	0.5899	1.098	53.28	....	.5079	24.2	.0671
Diluted cow's milk, 2.1% fat (Hoobler)	2.2155	0.7648	1.152	1.4507	67.0	.174	.3320	14.5	.040
Cow's milk, whole, 4% fat (Hoobler)	2.7418	0.59914	2.009	2.1426	78.1	.274	.1336	4.8	.0171
Cow's milk and cream, 5.4% fat (Hoobler)	2.2346	0.3789	1.336	1.8556	83.0	.235	.6196	27.7	.0657

Figures given above are in grams in 24 hours.

two very different forms, viz., that which is organically bound, occurring in milk, eggs and legumes, and a small part as phosphoric acid. When in organic combination it is found as nucleoalbumin, nuclein, vitellin, casein and lecithin.

The source in which we are most interested is that of mother's and cow's milk, and these two foods differ considerably in the amount of organically bound phosphorus. Mother's milk contains 0.31 to 0.45 gm. per liter of P_2O_5, while cow's milk contains 1.81 gm. P_2O_5 per liter. Keller[33] has shown that of the phosphorus of mother's milk 77 per cent. is organically bound, while in cow's milk only 27.9 per cent. is so bound. Of this organically bound phosphorus 54 per cent. occurs as nucleophosphorus in mother's milk, and but 13.4 per cent. in cow's milk, so that it is very evident that the phosphorus of cow's milk, though larger in actual quantity, is not in such form as to be available, as is the case of mother's milk. The nucleins of milk make up 41.5 per cent. of the total phosphorus of mother's milk, while of cow's milk only 6 per cent. is in that form. In mother's milk 35 per cent. of total phosphorus is in the form of lecithin, while the lecithin of cow's milk is but 5 per cent. according to Stocklasa.[34]

The form in which the phosphorus reaches the organism is important for Salkowski has shown that the organism has not the power to build from phosphorus-free albumin, or from inorganic phosphates, cells which require as an integral part organically bound phosphorus.

Indeed, it has been shown that the phosphorus absorption is not in the least affected by the presence or absence of inorganic phosphates, but, on the other hand, the phosphorus absorption may be greatly increased when a child is fed on yolk of egg as shown by Cronheim and Muller.[35]

Phosphorus is in demand in the body, particularly in glandular structures and bones, and for the central nervous system, and we should expect to find a considerable daily need on the part of the growing organism. This need seems satisfied in the healthy breast-fed infant on an intake varying from 0.7 to 0.8 gm. as a minimum and 1 to 2 gm. as a maximum. This is a wide variation, but we should consider that phosphorus is one of the minerals which becomes a definite part of the tissue structures throughout the body, and by virtue of its close connection with the albumin molecule must likewise suffer destruction along with the albumin, therefore it varies with the protein need.

33. Kellar, A.: Arch. f. Kinderh., xxix, Stuttgart, 1900, p. 1.
34. Stocklasa: Ebenda, 1897, xxiii.
35. Cronheim and Muller: Ztschr. f. diät. u. physik. Therap., 1903, vi.

The investigators who have determined phosphorus balances on infants are Blauberg, Michel, Keller, Cronheim and Muller and Schlossman. Let us consider some of their findings in comparison with the determinations which I have made.

ABSORPTION

It will first be noted that the intake of phosphorus is nearly ten times as great for cow's milk as for mother's milk and that in both forms of milk feeding the per cent. of intake absorbed indicates a very good absorption ability. In mother's milk, the absorption per cent. is 89.2 and that of cow's milk 53.2 in Blauberg's case. My determinations were 67.0 per cent., 78.1 per cent. and 83.0 per cent. on low, medium and high fat feeding. From this it would seem that phosphorus is more readily absorbed in the presence of increasing quantities of fat. The amount of the absorption depends more on the kind of phosphorus than on the quantity. The absorption of phosphorus is hindered when there is a relatively high ratio of accompanying alkaline earths and alkalies in the food; for example, when vegetables are fed a large calcium intake is present. This forms insoluble salts of phosphorus in the intestine and thus absorption is prevented. However, when these two elements meet within the body, they are joined in exceedingly close metabolic activity.

From my own determinations it appears that the phosphorus and nitrogen absorption varied considerably from the ratio in which these elements occurred in the food. Phosphorus absorption was relatively less than nitrogen absorption, during the low (2.1 per cent.) fat feeding, and was best in the medium fat feeding (4 per cent.), where it approximated the ratio which existed between nitrogen and phosphorus in the food.

RETENTION

The retention of phosphorus is one of great importance to the existence of life, for in conditions of starvation the organism clings tenaciously to its phosphorus—perhaps more so than to any other mineral constituent, except NaCl. This is probably due to its close connection with the central nervous system, for at the end of long periods of starvation the phosphorus content of nervous tissue is very little impoverished. This retention is, no doubt, in proportion to the need, and not only the present need, but it is stored up for an emergency; for the animal organism when fed on phosphorus-rich diet not only brings itself into phosphorus equilibrium, but retains a part of this excess phosphorus. The

retention keeps step with the need and gradually diminishes when the skeleton is well formed.

As in the case of absorption, the phosphorus is retained not so much in proportion to its amount as according to the kind present. Its retention runs parallel with that of nitrogen in cases studied by Keller,[33] but L. F. Meyer[36] has been unable to confirm this finding, and in my determinations phosphorus and nitrogen were not retained in proportional amounts, i. e., 29.5 per cent. food-nitrogen was retained while only 4.8 per cent. of food-phosphorus was retained.

ELIMINATION

The elimination of phosphorus takes place both through the feces and through the urine. In most instances it is about equally divided between these two channels of excretion. However, great variations occur, for example, in children on a vegetable diet which contains much calcium, the phosphorus is largely excreted through the feces, since the calcium forms insoluble salts with the phosphorus and thus absorption is inhibited, while children on a generous flesh diet will excrete most of the phosphorus through the kidneys. The amount excreted through the urine on mother's milk varied from 0.04 to 0.08 gm., while on cow's milk it was much higher, being 0.589 gm. in Blauberg's case and as high as 2.009 gm. in one of my determinations. (See phosphorus tabulations.)

In the feces from mother's milk feedings, the elimination varied from 0.02 gm. to 0.036 gm., while on cow's milk it was 0.962 in Blauberg's case. My own determinations were 0.7648, 0.5991 and 0.3789 gm., the larger quantity appearing with the lower fat-content of feeding and diminishing as the fat was increased.

A number of investigators have tried to show that the elimination of phosphorus and nitrogen was parallel, arguing from the fact that with cell destruction both N and P were released; and, indeed, this is true for certain groups of tissues, and could we estimate their catabolism separately, this would be our result. However, since N is only influenced in the protein wear and tear of the body, and since phosphorus has many influences other than is brought about by its connection with nitrogen in the albuminous molecule, as a number of observers have shown—Ehrstrom, and more recently L. F. Meyer[36]—there may be nitrogen retention with a phosphorus loss, and vice versa. The fact, too, that phosphorus is retained so tenaciously, while nitrogen is more readily given up, is

36. Meyer, L. F.: Ztschr. f. physiol. Chem., 1904, xliii.

another reason why the ratio of $N:P_2O_5$ in the urine is of little value as an index to cellular metabolism. The phosphorus balance obtained by considering the intake and elimination through feces and urine can only be depended on for correct interpretation of metabolic activity of phosphorus, and, indeed, the same may be held for any of the food constituents.

ANOMALIES IN PHOSPHORUS RETENTION

The anomalies related under the head of calcium retention are all shared in by phosphorus. Indeed, the pathologic conditions which affect one nearly always affect the other. As has been stated, in rachitis and osteomalacia there is a disturbance of retention of the phosphorus, particularly that part bound with calcium and magnesium. In these diseases the giving of calcium increases the retention of phosphorus and the giving of phosphorus increases the retention of calcium, proving undoubtedly their chemical and physiologic affinity.

Phosphorus has a close connection with intermediary metabolism, as shown by its large content in the thyroid gland, the ovaries and the testes. So great is the necessity for phosphorus in the functioning of the testes and ovaries that castration is sometimes employed in order to divert the phosphorus to the use of the bones, as has been done occasionally in osteomalacia.

In that anomaly known as phosphaturia, in which the ratio of P_2O_5 to CaO changes from 12:1 to 4:1, if a calcium-poor diet is given, the phosphates quickly disappear. Phosphorus may be retained in abnormally large quantities as pointed out by L. F. Meyer.[37]

SODIUM AND POTASSIUM

The relationship of potassium and sodium to the maintenance of the alkalinity is a very interesting and important one. The study of the influence of their *ions* on muscle-contractility and nervous irritability is yielding valuable data. The power of their *ions* to influence body weight, body temperature, pulse and even leukocyte count is a most important contribution made by L. F. Meyer[37] and S. Cohn.[23]

We will first discuss the problems of alkalinity into which Na and K enter, since these elements form the fixed alkalies. Under the anomalies of alkalinity we will discuss the problems which relate to variations of this alkalinity.

---

37. Meyer, L. F.: Deutsch. med. Wchnschr., 1905, No. 37.

It should be remembered that both alkaline and acid solutions exist within the same body; that the blood, various secretions, as well as each body cell has a definite amount of alkali, and can vary only within very narrow limits in order that they may perform their proper functions. This automatic regulation of alkalinity of the tissues and fluids is one of the marvels of the human mechanism, and it is remarkable how rarely it varies sufficiently to produce a pathologic condition. It is for the maintenance of this stupendously important work that the fixed alkalies, sodium and potassium, are used. Albu and Neuberg[28] have explained this self-regulation thus: Through the tearing down of the albumin of the body and the albumin taken in in the food, sulphuric and phosphoric acids are set free and must be neutralized by the alkalies of the blood. These acids would draw out the fixed alkalies were it not for the supply of carbonate derived from the carbonic acid and from the vegetable salts taken in the food. At certain times when the breaking down of albumin is excessive, ammonia is also set free and this is used along with the carbonates for the fixing of the acids. By means of this sort of neutralization, the acids become a constituent of the body, the fixed alkalies remain untouched, and the alkalinity of the tissues is unchanged. Should this reaction suffer the least change, either through a lessening of the bases or an increase of the autogenous acids, the organism becomes at once in danger.

The constant chemical reaction is also necessary for the ferment action which takes place throughout the body. The alkalies act also as carriers of the carbonic acid in the blood-stream.

The *ions* of potassium and sodium have an important bearing on the heart action, as shown by Overton.[38] K *ions* do not seem an absolutely necessary accompaniment of rhythmical action, but if present in too large numbers they cause a depression, even to complete inhibition. On the other hand, Na *ions* are necessary to contractility and irritability of heart-muscle. If present alone they produce muscular relaxation.

Jacques Loeb[26] has shown how closely developing life is dependent on exact proportions of NaCl in solution as shown by his experiments in sea-water, physiologic salt solution and in water with no NaCl in it.

Let us, therefore, study the sources of supply of these important elements, and see if we can determine the daily need for the growing infant. (See tabulation on page 25.)

38. Overton: Arch. f. d. ges. Physiol. Bonn (Pflüger), 1902, xcii, 346.

Potassium as K_2O

In 1,000 gm. mother's milk 0.69 gm. K_2O.
In 1,000 gm. cow's milk 1.885 gm. K_2O.

Food	Intake	Elimination		Absorption		Retention	
		Feces	Urine	Gm.	Per cent.	Gm.	Per cent.
Mother's milk (Klotz)	1.1032	0.2842	0.1591	....	....	0.6598	74.2
Cow's milk (Meyer)	1.9605	0.2033	1.4411	....	....	0.8161	16.12
Cow's milk (Blauberg)	1.57	0.271	1.12	1.30	82.8	0.180	11.5

Figures given above are in grams in 24 hours.

Sodium as Na_2O

In 1,000 gm. mother's milk there is .049 gm. Na_2O.
In 1,000 gm. cow's milk there is .465 gm. Na_2O.

Food	Intake	Elimination		Absorption		Retention	
		Feces	Urine	Gm.	Per cent.	Gm.	Per cent.
Mother's milk	0.5877	0.1924	0.1481	....	....	0.2471	67.2
Cow's milk	0.478	0.075	0.3305	....	....	0.0725	15.27
Cow's milk (Soldner)	0.409	0.098	0.343	.311	75.9	Negative	....

Figures given above are in grams in 24 hours.

In mother's milk there is much less sodium and potassium than in cow's milk. There is more potassium than sodium in each of these milks. The daily need of the nursing infant as represented by the intake is for sodium 0.5877 gm., and for potassium 1.1032 gm. In cow's milk feeding the sodium intake was below the intake on mother's milk and the potassium intake was considerably above that on mother's milk.

ABSORPTION

The absorption is relatively good on both milks. On absorption the Na salt takes its place in the blood and tissue fluids, while the potassium, displaying its selective action, takes its place in the various body-cells and in the blood-cells. Its most common salts are potassium phosphate, which is the chief mineral constituent of red blood corpuscles, and potassium chlorid, which is found in the body-cells. The potassium salts make up 0.4 per cent. of the total blood and 0.65 to 0.8 per cent. of fresh muscle tissue. It is evident therefore that for the production of the muscle of the growing child an adequate supply of potassium salts must be given.

RETENTION

The retention in per cent. of intake in mother's milk is very good, being 67.0 per cent. for sodium and 74 per cent. for potassium, while the retention on cow's milk is relatively poor, being 15.27 per cent. for sodium and 16.12 per cent. for potassium.

ELIMINATION

K and Na are eliminated through the urine and feces. The potassium in the urine is bound with Cl and with phosphorus and the sodium chiefly as NaCl. The sodium of the urine largely depends on the sodium intake in the food, while the potassium in the urine depends on the destruction of tissue; hence K metabolism is parallel with tissue destruction. This is explained by the fact that K is in the cells and is more closely bound, while Na is held in solution in the blood and tissue fluids and, therefore, more readily excreted. The normal ratio of Na to K in the urine is 3:1, 2:1 and some authors place it as 5:3.

ELIMINATION THROUGH THE FECES

About 15 to 25 per cent. of the intake of K and N are eliminated through the feces. These amounts vary considerably with the kind of diet, whether it is rich in alkali or not, or whether it is vegetable or made up of a considerable part of meat.

ANOMALIES OF RETENTION OF FIXED ALKALI

There is at times an over-retention of potassium salts to the point of potassium intoxication, and some authors[28] have attempted to build a theory for uremia on this fact. In such cases the potassium salts are retained in the blood-stream rather than taking their places in the tissue structure. But the most common anomaly is not that of over-retention but of marked withdrawal of the fixed alkalies. Against such a contingency the organism of the carnivora has builded up a strong resistance. First in the use of the carbonate of the tissue fluids and blood, and, as a last resort, in the production of ammonia. As has been previously stated, under normal conditions the carbonates with the help of a small amount of ammonia, are sufficient to care for the normal production of acids in the body. Under abnormal production of acids, as occurs in diabetes and in conditions of acidosis in certain infants fed on high fat mixtures, and in some older children fed on a mixed diet containing a quart or more of rich milk, there is a demand for a large quantity of ammonia to protect the fixed alkali.

A vast number of researches have been carried on covering the field of conditions of acidosis. It was Salkowski in his experiments on dogs who first pointed out that the self-produced body acids were bound by the withdrawal of the fixed bases of the body, and thus there would be impoverishment of these indispensable mineral constituents were it not for the fact that the carnivora are protected by this increased ammonia excretion; but this protection is only within narrow limits.

Not only is the withdrawal of alkali accomplished through the overproduction of acids, but it has been shown that a diet rich in fats will cause a withdrawal of alkali for the purpose of combining with the fatty acids of the stools. The fatty acids will first utilize such alkaline earths (Ca and Mg) as are available, and then for further neutralization will call on the fixed alkali of the body. This in turn demands the production of ammonia for the protection of the fixed alkali. This often occurs in healthy infants when on a high fat mixture, but it takes place preeminently, as shown by L. F. Meyer,[23] in the stage of decomposition of Finkelstein's *Ernährungstörung*. In this condition not only does the fat cause loss of alkali, but even sugar produces the same result.

SODIUM CHLORID

Of all the mineral constituents, sodium chlorid has the most varied and important functions to perform. The function of maintaining osmotic pressure has been the one most studied, and its relation to the

Chlorin as NaCl

In 1,000 gm. mother's milk, 0.294 gm. Cl.
In 1,000 gm. cow's milk, 0.82 gm. Cl.
In 1,000 gm. cow's milk (Hoobler), 1.8678 gm. NaCl.

		Elimination		Absorption			Retention		
Food	Intake	Feces	Urine	Gm.	Percent.	Per Kilo	Gm.	Percent.	Per Kilo
Mother's milk	0.3297	0.0135	0.1776	0.3162	95.4	....	0.1386	58.0	....
Diluted cow's milk, 2.1% fat ..... (Hoobler)	2.3178	0.042	2.2421	2.2758	98.1	.274	0.0337	1.4	.004
Whole cow's milk, 4% fat ..... (Hoobler)	2.3926	0.1567	2.3328	2.2359	93.4	.286	Negative	....	....
Cow's milk and cream, 5.4% fat.... (Hoobler)	2.3428	0.06031	2.1340	2.2824	97.3	.288	0.14849	6.3	.018

Figures given above are in grams in 24 hours.

retention and excretion of water is well known. In recent years to the Na *ions* and the Cl *ions,* acting either separately or in conjunction, have been assigned various results. L. F. Meyer[23] has shown that the intake of Na *ions,* especially when bound with the halogen group, particularly with chlorin, when in certain concentration, viz., 3 gm. NaCl to 100 c.c. water, always produced an increase of temperature in a young infant. There is a marked decrease in the body weight when fed on milk freed of salts; also the pulse and leukocyte count are affected. Just what the daily need of this salt is depends largely on the kind of food ingested. There is a certain demand for this salt and when the intake is cut off the body retains with great tenacity what it has until further intake occurs.

The chlorin intake in mother's milk is 0.3297 gm., while on cow's milk the chlorin intake in terms of NaCl was 2.3926. The tabulation on page 133 shows the chlorin metabolism in terms of NaCl.

The demand for NaCl is greater in herbivora than in carnivora, because of the greater consumption of K carbonates, as was pointed out in the classic observation by Bunge.[39] His concise explanation of this phenomenon is that with a large intake of K carbonate there is formed in the blood the salts of sodium phosphate and potassium chlorid. Both being foreign, they are eliminated, leaving a loss of NaCl which must be replenished.

NaCl is ingested in large quantities. It being well absorbed, there is an increased quantity in the blood, hence its isotonicity is disturbed and either there must be a holding back of water until the solution is isotonic, or an increased elimination of the NaCl. Both of these processes may take place.

ABSORPTION

The absorption of salt is found to be excellent—usually above 90 per cent. of the intake is absorbed. The retention of NaCl is only sufficient to cause a balance to be maintained under normal conditions. In my determinations I found that there was utilized but 1.4 per cent. to 6.3 per cent. of the intake.

ELIMINATION

The elimination takes place almost entirely through the kidneys. But a very small quantity appears in the feces, so well is it absorbed. In my determinations there was a little over 2 gm. excreted through the urine daily, while less than 0.1 gm. appeared in the feces.

39. Bunge: Cited by Albu and Neuberg, Mineralstoffwechsel, p. 164.

It has been observed that salt solution when injected subcutaneously is more quickly eliminated than when taken by mouth. With the excretion of NaCl there must accompany it a certain amount of water, and, therefore, the intensity of diuresis depends on the molecular concentration within the body. Not only does salt affect the retention and withdrawal of water, but it holds a very close relation to nitrogen.

Voit's original work seemed to show that with increasing retention of NaCl there was an increased retention of nitrogen; later investigations have not agreed with this. Belli[40] sums up his findings with the statement that in small amounts, as in the food normally, it hastens and increases protein retention, but in greater quantities it tends to lessen the nitrogen retention.

THE ANOMALIES OF NaCl RETENTION

There are a number of conditions which seem markedly affected by sodium chlorid. The most important is that of nephritis. Von Noorden[41] was the first to work on this important condition. He noted a variation in different cases. Some retained and others did not retain NaCl. Halpern[42] has shown that both in acute and chronic nephritis the salt content of the urine is dependent on the salt content of the food. In cases in which there is edema there is marked lessening of the edema when the patient is put on a salt-free diet, and there appears in the urine an increase in the NaCl elimination. The use of salt-free diet, whether with or without edema, brings about more or less of a dechloruration of the body. It would seem that in these cases the NaCl retention always precedes the water retention and that the edema consequent on water retention is due to the NaCl retained. However, no hard and fast rules can be laid down in regard to use of salt-free diet, as in some cases it will not reduce edema, and in some cases a salt-rich diet will not always produce NaCl retention.

L. F. Meyer[23] believes that many of the symptoms present in food disturbances of infants may be traced to the deleterious influence of sodium chlorid, acting not only as salt, but also in the capacity of the respective *ions*. He believes particularly that the rises of temperature during the stage of intoxication of Finkelstein's *Ernährungstörung* is

40. Belli: Cited by Albu and Neuberg, Mineralstoffwechsel, Berlin, 1906, p. 170.

41. Von Noorden: Lehrbuch d. Pathologie d. Stoffwechsels, Berlin, 1893.

42. Halpern: Cited by Albu and Neuberg, Mineralstoffwechsel, Berlin, 1906, p. 174.

due to the action of these *ions*. In children with food disturbances smaller quantities of NaCl solution will raise temperature more quickly than in healthy children.

Fisher[43] has shown that the injection of salt solution of one-sixth molecular strength may produce glycosuria, and that this glycosuria may be stopped by injecting a calcium chlorid solution.

Abderhalden[6] believes that every cell has particular salts in specific apportionment and that a disturbance of this relation, as would take place in Fisher's experiment just quoted, would cause considerable trouble in the life processes of the cell.

SULPHUR

Of all the mineral salts, sulphur has been the last to receive due attention at the hands of investigators. What we know of sulphur metabolism is largely due to Freund[46] and his pupils. Sulphur presents itself for ingestion in the food in two different forms, viz., in the inorganic salts, and organically bound with albumin. The inorganic salts have little or no effect on metabolism and need not be considered. It is that sulphur which is organically bound which is the important part and which supplies the daily need of the growing infant.

Whether or not sulphur is necessary for the maintenance of life is still a question, but any substance so closely associated with nitrogen may be assumed to have a distinct function, though as yet this function is obscure.

The total sulphur intake of infants fed on mother's milk is .04 gm., while on cow's milk the daily intake is about 0.44 gm., according to my recent researches. The sulphur of mother's milk is very well absorbed, as is also that of cow's milk. My determinations show that it is absorbed in from 88.2 to 95.7 per cent. of intake. This absorption is quite in keeping with the facility with which nitrogen is absorbed, and this is probably due to the fact that its connection with the albumin molecule is so close. (See tabulation, page 77.)

The absorption takes place through the small intestine, and some of it is again eliminated into the large intestine, making up the sulphur found in the feces.

---

43. Fisher: Cited by Abderhalden, Lehrbuch d. physiolog. Chemie, Berlin, 1909, p. 358.

46. Freund: Zeit. f. phys. Chem., Strassburg, 1900, xxix, 24-46.

Sulphur in Terms of S

In 1,000 gm. mother's milk, total sulphur .0572 gm.
In 1,000 gm. cow's milk (Hoobler), total sulphur .33538 gm.

Food	Intake	Elimination		Absorption			Retention		
		Feces	Urine	Gm.	Percent.	Per Kilo	Gm.	Percent.	Per Kilo
Mother's milk	.0396	.0096	.026	.0298	75.5	....	.0039	9.8	....
Cow's milk	.5832	.01484	.2019	.0436	74.5	....	Negative	....	....
Diluted cow's milk, 2.1% fat (Hoobler)	.46308	.0542	.3777	.4089	88.2	.491	Negative	....	....
Whole cow's milk, 4% fat (Hoobler)	.4411	.02430	.26589	.4168	94.2	.531	.15091	34.2	.019
Cow's milk and cream, 5.4% fat (Hoobler)	.4444	.01901	.30585	.42546	95.7	.533	.11961	26.9	.015

Figures given above are in grams in 24 hours.

Schwarz[47] found in a 5-year-old child on a mixed diet that the absorption was very good, being 92.2 per cent. of the intake. My normal child on a milk diet had an absorption of 92.4 per cent. of the intake. Identical methods of determination were used by both of us.

RETENTION

The retention of sulphur in mother's milk feeding is very good, while with cow's milk the retention is relatively poor. In one of my determinations there was a negative balance and in two others 34.2 and 26.9 per cent. of the intake was retained. Schwarz,[47] in a normal 5-year-old child on a mixed diet found that sulphur retention was relatively poor, being 31.1 per cent. of the intake.

ELIMINATION

The elimination of sulphur occurs mostly through the urine. In cow's milk feeding ten times as much appeared excreted through the urine as through the feces.

The sulphur in the feces appears as iron sulphate and alkali sulphate, while in the urine there are recognized four different forms, viz., the inorganic sulphate sulphur, the ethereal sulphate sulphur, neutral sulphur and basic sulphur. The first named is by far the most abundant in the urine, making up about 80 per cent. of the total sulphur. Ethereal sulphate sulphur makes up about 8 per cent. of the total sulphur and the neutral and basic sulphurs the balance.

Just what significance should be assigned to total sulphur and to each of the various sulphurs making up the total, has been the subject of much speculation.

Because of the connection between sulphur and albumin in tissues, the sulphur metabolism has been taken as the index to protein metabolism. The normal ratio is $N : H_2SO_4 : : 5 : 1$.

The relative amount of ethereal sulphate sulphur has been taken as an index of the degree of albuminous putrefaction going on in the intestine, and also for the breaking down of albuminous cells in the body.

The neutral sulphur appears to be increased on a vegetable diet and decreased on a meat diet. Investigators have shown that in periods of starvation, as well as in other conditions of protein break-down, there is an increase in the per cent. which neutral sulphur holds to total sulphur. Lepine[48] is the authority for believing that neutral sulphur has its origin

47. Schwarz: Jahrb. f. Kinderh., 1910, lxxii, p. 549.

partly from the taurin of the bile. This is first excreted into the intestine, reabsorbed, and again eliminated through the urine. In those conditions of disturbed oxidation, if below normal, neutral sulphur is low; if above normal, then the neutral sulphur is increased. In my determinations of neutral sulphur it appears that on cow's milk containing 2.1 per cent. fat the neutral sulphur averaged 7.2 per cent. of the total sulphur, but that on feeding 4 per cent. and 5.4 per cent. fat mixtures the neutral sulphur was increased to as high as 15 per cent., more than doubled. This might be explained by the fact that during these higher fat feedings small amounts of acetone, diacetic acid and beta-oxybutyric acid were found in the urine, forecasting an impending acidosis, in which already tissue albumin had begun to disintegrate.

ANOMALIES OF SULPHUR RETENTION

Schwarz has shown that in rachitis the total sulphur absorption in two cases was 76.9 and 83 per cent., which was somewhat lower than in his normal case, which showed 92.2 per cent. absorption. The retention in one case was 30.9 per cent. and in the other 26.1 per cent. of the intake. This was about the same as in his normal case, viz., 31.1 per cent.

There was eliminated through the urine 55 per cent. of the total sulphur in one case and 54.1 in the other, while in the urine of his normal case 61.1 per cent. was thus eliminated. The elimination by the feces in two of his cases of rachitis showed a marked change from his normal case—23.1 per cent. and 17 per cent. in rachitis and but 7.8 per cent. in the normal.

Of the various forms of sulphur in the urine, the only one which showed much variation from the normal was that of the neutral sulphur, which in two of his cases was considerably increased, being 18.5 per cent. and 18.6 per cent., while his normal showed 7.8 per cent. of the total sulphur. In one of his rachitic cases no variation from the normal occurred.

A further anomaly of sulphur metabolism is that of cystinuria. Bunge has shown that in the catabolism of cystin, albumin, which has sulphur in it, sets sulphur free, which usually unites with bases and is eliminated as sulphates; but if the bases are lacking, then alkali is drawn from the cells of the body.

---

48. Lepine: Cited by Albu and Neuberg, Mineralstoffwechsel, Berlin, 1906, p. 148.

SUMMARY

1. Salts are necessary to maintain life.

2. Salts are best absorbed and utilized when in organic combination with food stuffs.

3. There are marked differences in the salt content of mother's and cow's milk which should be considered in artificial feeding.

4. Certain pathologic conditions arise in which certain of the salts are not absorbed, even though in abundance in the food.

5. In certain other pathologic conditions salts are actually withdrawn from the body to such an extent as to impoverish the organism and produce grave disturbances of nutrition.

6. The various salts, with the exception of iron, are present in sufficient quantities and proper proportions in mother's milk. In most of the dilutions of cow's milk there is an excess of salts which may be neglected in feeding normal infants, but which plays an important rôle in the feeding of children already suffering from nutritional disturbances. The conditions under which the salt content of feedings should be altered and in just what degree each or all should be varied, are still unsolved problems.

131 East Sixty-Seventh Street.

STUDIES IN THE METABOLISM OF ATROPHIC INFANTS *

CHARLES A. FIFE, M.D., AND BORDEN S. VEEDER, M.D.

PHILADELPHIA

The value of a food for an infant depends, in the broadest sense, on two factors: on the one hand, whether or not the food meets the requirements of the organism in furnishing sufficient energy and material for growth, and on the other, whether or not the food itself, or the substances derived from it in the process of digestion, exert any deleterious action on the organism.

Fundamentally associated with the first problem is the question of absorption of the food in the gastro-intestinal canal. In our system of infant feeding in which the percentage of protein, fat and carbohydrate in the food is the criterion by which we judge of its suitability, and by which we modify the mixture according to the clinical manifestations, it is important to know whether the absorption of the different substances is influenced by the percentage relation of one to another. Very few observations have been made on this point. The following studies on atrophic infants were undertaken with the purpose of determining the absorption of fat under the influence of different proportions of fat and carbohydrate, and the influence of the varying quantities of fat and carbohydrate on the nitrogen metabolism.

The methods used were as follows:

The infants were given a definite formula for periods of at least six days, and during the last three days of each period the urine and feces were completely collected. The fat and nitrogen content of the food was determined each day during the periods by analysis. As the carbohydrate excretion was not considered, the sugar intake was not accurately determined, but was computed from the average found in many previous analyses of milk, plus the amount of a 1 per cent. lactose solution added to bring the formula to the desired strength. As will be seen later, it was only necessary to know the approximate quantity of sugar, i. e., whether the sugar percentage was high or low. The urine was preserved by chloroform and kept on ice until the three-day specimen was completed.

* From the William Pepper Clinical Laboratory, University of Pennsylvania.

TABLE 1.—DATA CONCERNING EXPERIMENT IN CASE 1 TO DETERMINE FAT ABSORPTION.

Date	Milk Formula	Fat, gm.	Sugar, gm.	Protein, gm.	Amt. each feeding ounces	No. of feedings	Beginning weight	End weight
			PERIOD I					
2/27 to 3/4	3.5—6.5 —2.5	135.	235.	83.	6	7	10 lbs. 9 oz.	10 lbs. 11 oz.
Stools yellow, soft, mushy; no curds.								
			PERIOD II					
3/4 to 3/10	3.2—1.75—2.	115.	68.	57.4	8	7	10 lbs. 11 oz.	10 lbs. 11 oz
Stools yellow, formed no curds.								
			PERIOD III					
3/10 to 3/16	1.2—6. —2.5	57.	80.	89.28	7	7	10 lbs. 11 oz.	10 lbs. 15 oz.
Stools yellow, fairly well formed; few small white curds.								
			PERIOD IV					
3/16 to 3/22	1.2—6. —2.5	57.	273.4	89.28	7	7	10 lbs. 15 oz.	11 lbs. 2 oz.
Stools semi-liquid, greenish, few rather large white curds.								

TABLE 2.—DATA CONCERNING EXPERIMENT IN CASE 2 TO DETERMINE FAT ABSORPTION.

Date	Milk Formula	Fat, gm.	Sugar, gm.	Protein, gm.	Amt. each feeding ounces	No. of feedings	Beginning weight	End weight
			PERIOD I					
2/27 to 3/4	3. —6. —2.	141.	270.	76.5	7	7	11 lbs. 10 oz.	11 lbs. 14 oz.
Stools soft, liquid yellow; no curds.								
			PERIOD II					
3/4 to 3/11	3. —2. —2.	145.8	80.	67.1	7	7	11 lbs. 14 oz.	12 lbs. 3 oz.
Stools liquid, yellow, no curds.								
			PERIOD III					
3/11 to 3/16	1. —2. —2.5	57.	80.	89.28	7	7	12 lbs.	12 lbs. 1 oz.
Stools soft, semi-liquid, greenish-yellow.								
			PERIOD IV.					
3/16 to 3/22	1. —6. —2.5	137.	273.56	89.28	7	7	12 lbs. 1 oz.	12 lbs. 6 oz.

The total three-day specimen of feces was evaporated to dryness in the usual manner. By using a three-day period after giving the same formula from three to six days previously, the chances of error from irregular excretion, as at times occurs in twenty-four-hour specimens, are largely eliminated. *It is to be especially noted that the figures throughout represent the combined total of three consecutive days and not the daily intake or excretion.*[1]

The histories of the cases studied and the notes of the different periods are as follows:

CASE REPORTS

CASE 1.—Albert H., white, aged 9 months, was admitted to the hospital early in January for acute bronchitis, which cleared in a few days; previous history of gastro-enteritis and malnutrition; bottle-fed (milk modifications unknown) since shortly after birth; father tuberculous and mother mentally deficient. On admission the child weighed 10 pounds, 7 ounces, and at the time of beginning the studies was nine months old and weighed 10 pounds 8 ounces. During the intervening two months the weight remained almost stationary, although numerous milk modifications were tried. The stools were soft, greenish or yellow in color and contained occasional curds. Physical examination showed a child with flabby musculature and little adipose tissue; cannot sit alone; length 25 inches; circumference of head 16 inches; circumference of chest 15½ inches; circumference of abdomen 15 inches; anterior fontanelle open, measures 1¼x1½ inches; superficial lymph-nodes slightly palpable; slight beading of the ribs; heart and lungs negative; abdomen soft and not distended; reflexes normal.

CASE 2.—Edward, white, aged 10 months, was admitted to hospital Jauuary 8 for diarrhea and loss of weight, with a previous history of malnutrition with loose and offensive stools. The child was bottle fed after two months; had diphtheria at four months followed by discharging ear; family history negative. On admission he weighed 10 pounds, 10 ounces. Under treatment the ear condition improved and the stools became much better in character, being as a whole yellow in color and smooth, with only occasional curds. The weight curve was fluctuating and between the time of admission and the first period the net gain was only one pound; age at time of beginning studies (Feb. 27), 10 months; weight 11 pounds, 10 ounces. Physical examination showed slightly rachitic, atrophic infant, with flabby musculature. He could hold his head upright, but could not sit alone.

Circumference of head 17 inches, chest 15 inches, abdomen 16½ inches. Anterior fontanelle open—1 inch in width; heart and lungs negative; liver slightly enlarged; umbilical hernia; posterior cervical lymph-nodes enlarged; reflexes normal.

1. Fat in the milk was determined by the Leffman-Beam method and nitrogen by Kjeldahl. The nitrogen of the urine and of the feces was determined by the Kjeldahl method, and Ca by the method of McCrudden. In the fat extraction from the feces the method of Brugsch was used, which permits of a separation of the soaps from the neutral fats and fatty acids.

FAT ABSORPTION

The work that has been done on the absorption of fats in infants is a difficult subject to review and correlate. There are apparently many discrepancies in the results of the studies of fat metabolism that have been published, which we believe in the first place depend largely on the methods used. Kumagawa and Sutro[2] have recently studied this question, using known quantities of fat, and find considerable differences in the results obtained by several of the methods in common use. They have worked out a method which gives the most accurate results for total quantities of fat, but which does not permit of a separation of the fat in the feces into its component parts; i. e., neutral fats, fatty acids, and soaps. This is of considerable importance in the study of the feces in infancy, as it is supposed to bear an intimate relation to the question of the diseases of salt metabolism (rachitis, tetany, exudative diathesis, etc.). While the method we used gives results which probably vary from 5 to 10 per cent. from the total quantity of fat, the same error is carried throughout, and as the studies are comparative in nature this error is of little importance. It is also difficult to contrast the results of one worker with those of another, for although the studies as a whole are numerous, the conditions under which they have been undertaken differ considerably and the investigations are few in which any one point or question has been under consideration. A normal breast-fed or artificially fed infant absorbs the larger part of the ingested fat. Bahrdt,[3] in the most recent and careful studies that have been made, using the Kumagawa method, finds an absorption of 93 per cent. in the normal child. A few years ago Freund[4] reviewed the various studies on fat absorption and from these and others since published it may be concluded that the normal absorption in a healthy infant lies between 90 and 95 per cent. The figures outside of these limits published as "normal" are probably due to either faulty methods or to disturbances in absorption. In both acute and chronic nutritional disturbances absorption of fats in the intestine is lowered, from 10 to 50 per cent. or more of the amount ingested being found in the stool. Practically all of this fat is derived directly from the food, a very small amount of ether-extractable substances being found in the stool with a fat-free diet. The loss of fat in nutritional disturbances is due to several factors, as altered digestion, accelerated peristalsis,

2. Kumagawa and Sutro: Biochem. Ztschr., 1908, viii, 337.
3. Bahrdt: Jahrb. f. Kinderh., 1910, lxxi, 249.
4. Freund: Ergebn. d. inner. Med. u. Kinderh., 1909, iii, 38.

admixture with mucus, etc. In our own cases the loss was from 15 to 33 per cent. of the quantity ingested. There is some question as to the form in which the fats are absorbed from the intestinal canal, but it is the generally accepted view that they must be split before absorption and are then recombined in the cells of the intestinal mucosa.

Our problem, however, did not deal so much with the question of how much was absorbed, or the form in which it was absorbed, as with the question of the absorption of large and small quantities of fat, and the influences of varying quantities of carbohydrate on the absorption of the fat. The accompanying table (Table 3) summarizes our results as regards the first question.

TABLE 3.—SHOWING THE PERCENTAGE OF FAT LOSS IN THE TWO EXPERIMENTAL CASES DURING THE FOUR PERIODS

	Fat in Food Gm.	Fat in Feces Gm.	Fat Loss Per cent.
Case 1—			
A Period I	135	20.08	14.9
Period IV	57	18.89	33.0
B Period II	115	21.21	18.0
Period III	57	14.05	24.6
Case 2—			
A′ Period I	141	23.18	16.5
Period IV	57	18.86	33.0
B′ Period II	145	29.53	20.2
Period III	57	18.95	33.0

When large quantities of fat are given the actual amount of fat in the stool is increased but the percentage absorption is much better. Average figures show this clearly.

	Per-Cent of Fat in Mixture	Fat in Food Gm.	Fat in Feces Gm.	Fat Loss, Per Ct,
Case 1	3+	125	20.65	16.0
	1	57	16.47	28.9
Case 2	3+	143	26.36	18.4
	1	57	18.90	33.

In the 3 per cent. mixtures nearly five-sixths of the ingested fat was absorbed, while in the 1 per cent. mixtures a third was passed in the stool. Or, looking at it from another view-point, although there was about two and one-half times as much fat present in the food in the high fat periods, the feces contained only half again as much as in the low fat periods.

Somewhat similar results were obtained by Hecht[5] in a 12-months-old child in two three-day experiments:

	Fat in Food Gm.	Fat in Feces Gm.	Fat Loss Per Cent.
Period I	89.28	4.929	5.3
Period II	10.26	1.662	16.3

In this case, however, there was considerable stimulation of the intestinal mucosa when the low fat was given (Milchmalzsuppe made with Magermilch). During this period the child passed from five to six liquid stools daily and the two investigations may have different interpretations although similar in results. L. F. Meyer[6] likewise observed a difference in proportion between the fat intake and the loss in the feces (normal child):

	Fat in Food Gm.	Fat in Feces Gm.	Fat Loss Per Cent.
1.	10.97	0.8	2.29
2.	35.95	1.588	4.44
3.	44.3	1.75	3.95

Freund[4] gives a similar comparison between normal infants:

	Fat ingested Daily, Gm.	Fat in Feces Gm.	Fat Loss, Per Cent.
Experiment 1—			
Period I	3.93	0.4468	14.27
Period II	16.50	2.4160	14.64
Experiment 2—			
Period I	3.17	0.5785	18.25
Period II	15.90	2.2590	14.21

In this case the fat loss in the feces bears the same percentage relation, with high and low fat intake. There are so many points of difference (age, method, time, etc.) between our observations and those of Freund that we do not wish to draw conclusions from a comparison between the two.

As fat and carbohydrate differ from protein, in that they may be substituted for one another within certain limits, as both are energy and heat producers rather than tissue builders, we combined high and low carbohydrate diets with the fats in order to determine whether the amount of carbohydrate exerted any influence on the absorption of fats. Thus in Table 3 in the periods grouped under A and A′ the food contained a high

5. Hecht: Wien. klin. Wchnschr., 1907, xx, 497.
6. Meyer, L. F.: Biochem. Ztschr., 1908, xii, 422.

(6) percentage of sugar. In those grouped under B and B′ the food contained a relatively low (2 per cent.) amount. The total amounts are given in the accompanying Table 4.

TABLE 4.—HIGH AND LOW CARBOHYDRATE DIETS COMBINED WITH FATS TO DETERMINE INFLUFNCE OF CARBOHYDRATES ON FAT ABSORPTION

	Gm.		Gm.
Case 1—			
A Period I	235	B Period II	68
Period IV	273	Period III	80
Case 2—			
A′ Period I	270	B′ Period II	80
Period IV	273	Period III	80

Contrasting A with B, the A′ with B′ in Table 3, and considering the marked difference in the amount of carbohydrates in these periods, we are unable to find any apparent influence of the amount of carbohydrate on the absorption of the fat. Practically the same relation holds between the intake and absorption of large and small quantities of fat no matter whether a large or a small quantity of carbohydrate is present in the food.

As the quantity of nitrogen (see Table 6) in the food was nearly the same in all of the periods the explanation of these changes then must lie in the digestion of the fat itself. In no period was there a diarrhea present which might have accounted for the conditions. Moreover, the tolerance for or ability to absorb fat does not seem to be affected. In Case 1 there was an absolute absorption of 115 gm. of fat in Period I, while in Period IV the total quantity given was only 57 gm., of which a third (18.86 gm.), was found in the stool, only 1.2 gm. less than in the first period. A similar condition was present in Case 2. In none of the periods was the so-called "soap stool" of Czerny's "milk injury" or Finkelstein's "balance disturbances" present. We investigated, however, the question of soaps and calcium excretion and the results are shown in Table 5.

TABLE 5.—SHOWING DETERMINATION OF SOAPS AND CALCIUM

	Milk Formula	Fat in Stools	Soap	Soaps Per	Ca
		Gm.	Gm.	Cent.	Gm.
Case 1—					
Period I	3.5—6—2.5	20.08	2.57	12.3	3.54
Period II	3.2—2—2.	21.21	2.00	9.4	2.51
Period III	1. —2—2.5	14.05	6.13	43.6	2.51
Period IV	1. —6—2.5	18.89	6.30	33.3	3.95
Case 2—					
Period I	3. —6—2.	23.18	3.58	15.2	3.54
Period II	3. —2—2.	29.53	2.29	7.4	4.21
Period III	1. —2—2.5	18.95	10.66	56.2	3.72
Period IV	1. —6—2.5	18.86	9.90	52.5	3.74

In both cases the absolute quantity of soaps was about three times more in the low fat periods than in the high, and the relative amount was increased on an average nearly five times. The amount of Ca excreted in the feces bears no relation to the absolute amount or relative proportion of soaps. If in these cases the infants were atrophic as a result of fat injury, the high fat periods should have shown the higher amounts and percentages of soaps. An explanation on these grounds, then, is wanting. Birk and Rothberg thought the formation of fat stools depends on the withdrawal of the earthy alkalies through their combination with fat, and they see in this withdrawal the cause of the failure to gain weight in this condition. Freund contends that the amount of soap formation depends on the reaction of the stool, which in turn depends on the bacterial changes producing fermentation when large amounts of sugar are present. A study of Table 5 shows that in Periods I and II, with a high and a low sugar intake, the soap formation was low, and that in periods III and IV, with a low and a high sugar intake, the amount of soap is high, averaging 48 per cent. (Case 1) and 54 per cent. (Case 2) of the total quantity of fat in the stools. Moreover, the amount of Ca in the feces does not bear any relation to the amount of soaps present, whether we compare it with the actual amounts of soap or the percentage relation to the total amount of fat.

We must conclude, then, that the changes are due to certain unexplained factors and that they do not support any of the above mentioned studies on fat metabolism in chronic nutritional disturbances.

NITROGEN METABOLISM

The second part of the study took up the question of the nitrogen metabolism under varying fat and carbohydrate percentages and in this we have confined ourselves to the nitrogen retention. It is a generally accepted fact that the amount of nitrogen in the feces is not proportionate to nor dependent on the amount of nitrogen in the food, although when increasing the food nitrogen from a very low or hungering period there is an increase of nitrogen in the feces. In investigations made by Kellar[7] on fasting infants an excretion of nitrogen in the feces of 0.0716 gm. and of 0.097 gm. in twenty-four hours was found after a preliminary period of thirty hours. In artificially fed infants the nitrogen amounts from 2 per cent. to 6 per cent. of the total weight of the dried feces.[8] Very

7. Kellar: Arch. f. Kinderh., 1900, xxix, 123.
8. Hecht: Die Feces des Säuglings, 1911, p. 24.

little if any of the ingested nitrogen of the proteins is excreted as such although some of the nitrogen occurs in the form of their cleavage and putrefactive products. This together with the nitrogen of the gastro-intestinal juices and secretions, bacteria and epithelial cells, constitute the sources of the nitrogen of the feces. Although not directly dependent on the ingested food, it may be modified to some extent by the action of the food in stimulating or retarding the secretion of the gastro-intestinal juices, as the observations of Wohlgemuth and others have shown, it is very probable that, as in the case of Ca salts, the nitrogen absorbed may be excreted and reabsorbed in the intestinal canal. A glance at Table 6 shows no evident relation between the varying percentages of the food elements and the amount of nitrogen in the feces (i. e., nitrogen absorption). In Case 1 the amount varies from 1.345 gm. to 2.460 gm., while in Case 2 it is uniformly about 2.5 gm. in all four periods. For these reasons a study of the absorption is of little or no value and the important question is the study of the nitrogen retention. The nitrogen intake and the output in the urine and feces is shown in Table 6. The balance is considered as retained nitrogen, no account having been taken of the amount excreted through the skin. This is a small factor and in all probability would have been parallel throughout the periods in each case. So far as we know the only studies that have taken this into account are those of Rubner and Heubner,[9] and Tangl.[10] The former found a loss of 0.189 gm. of nitrogen per day in a normal child and 0.0338 gm. in an atrophic infant, while the latter found an excretion of 0.044 in an artificially fed infant.

The nitrogen retention may be studied in two ways, either the total percentage retention (Nutzungswerth) or the retention per kilo of body weight. The figures for the latter (last column, Table 6) have been divided by three so as to give the retention per kilo per twenty-four hours, in order to compare our figures with those of previous studies. It will be noted that in all of our periods the retention of nitrogen was very good. The nitrogen intake in all of the periods was higher than was necessary for the development and replacement of the body tissues. Although it was our intention to have the nitrogen intake the same in all periods, the total amount by analysis was less in Period 2 in each case.

9. Rubner and Heubner: Ztschr. f. Biol., 1899, xxxvii, 315.
10. Tangl: Arch. f. d. ges. Physiol., Bonn (Pflüger), 1904, clv, 453.

TABLE 6.—SHOWING NITROGEN INTAKE AND OUTPUT IN THE URINE AND FECES

Period	N in Food	N in Feces	N in Urine	N Retained	Per cent. of N Retained	Retention per Kilo per 24 Hrs.
Case 1—						
I	13.460	1.345	5.080	7.035	52.2	.482
II	9.185	1.418	5.174	3.593	39.2	.246
III	14.285	1.968	7.812	5.505	38.8	.370
IV	14.285	2.460	6.506	5.239	36.6	.349
Case 2—						
I	12.243	2.144	4.340	5.759	47.0	.351
II	10.722	2.550	5.660	2.512	23.4	.152
III	14.285	2.438	6.930	4.917	34.4	.298
IV	14.286	2.610	4.700	6.975	48.8	.416

In both of these periods the absolute retention is less although the percentage retention in Case 1 is practically the same as in Periods III and IV. It is evident that an increase of the nitrogen in itself leads to increased retention, but this opens a question which is outside of the scope of the paper. The highest percentage and best absolute retention is found in the high carbohydrate periods (I and IV). This is seen clearly in Case 2 in which the retention in the high periods averages 48 per cent. and 29 per cent. in the low. In Case 1 it is less marked as the difference between the averages is only 5.4 per cent., although Period I shows the highest percentage retention of all — over half of the ingested nitrogen being retained in the body. This is not due to insufficient calories in the food in the low carbohydrate periods, as between 75 and 80 calories per kilo were present in the food in Period III, which is the lowest period from the standpoint of calories. This observation is in accordance with those of Kellar and of Orgler. Orgler[11] studied the influence of lactose and saccharose on the nitrogen retention in a normal child and his results are summarized as follows:

Food	Food-N	Urine-N	Balance	Per Cent. Retained
300 gm. milk	1.7748	1.2853	+0.229	12.9
250 gm. malzsuppe	.....	.....	.....	....
10 gm. lactose	.....	.....	.....	....
10+50 gm. lactose	1.6743	.6824	+0.583	34.8
10+50 gm. saccharose	1.8272	.8369	+0.663	36.3

Kellar's[12] case is less conclusive, as the kind of food was completely changed, although the carbohydrates were markedly increased and the nitrogen remained practically the same:

11. Orgler: Jahrb. f. Kinderh., 1908, lvii, 383.
12. Kellar: Malzsuppe, eine Nahrung für Magendarmkranke Säuglinge, Jena, 1908.

Food	Food-N	Urine-N	Balance	Per Cent. Retained
½ milk c.mm. water	2.6725	2.0274	—0.2646	9.9
Malzsuppe	2.3443	1.4463	—0.417	17.8

As regards the quantity of fat in the food, we may simply state that as far as these observations show it is without apparent influence on the nitrogen retention. In comparing the nitrogen metabolism of the atrophic infants with that of healthy artificially fed infants we find a paucity of studies suitable for such purposes as a result of the variations in body weight and in the kind and amounts of foods used. The best suited for this purpose may be taken from Hoobler's[13] study of a nine months' infant weighing about 8 kilos. Three periods of three days each with a high, medium and low fat percentage, with a nitrogen intake of 20.7 gm., 21.6 gm., and 25.5 gm., respectively, were studied.

The nitrogen retention per kilo of body weight per day was as follows:

Low fat	0.362
Medium fat	0.270
High fat	0.285

Hoobler found that about 33 per cent. was retained in each of the periods; in other words, the amount of fat was of little influence. He thought the retention of nitrogen was not influenced by the amount ingested — a conclusion we do not feel is justified by his studies. Hoobler does not give the percentage of carbohydrate in his milk mixtures, but it is probable that they contained about 6 per cent. as is customary in most of the milk mixtures in this country. Comparing our periods of high (6 per cent.) sugar with his we find a much higher percentage retention as well as a better absolute retention:

	Case 1	Case 2
Period I	.482	.351
Period IV	.349	.416

The better nitrogen retention of the atrophic infants may be due to their beginning on a period of convalescence, as both children started in to improve from the moment they were placed on the metabolic bed in the first period.

SUMMARY

In the study of these two cases of infantile atrophy — the results of which are similar — the following conditions were noted:

The fat absorption was less than in normal infants, although the infants were able to absorb large quantities of fat.

13. Hoobler: Arch. Pediat., 1910, xxvii, 853.

The percentage absorption was better with a large amount of fat in the food than with low amounts.

The amount of carbohydrate in the food did not influence the fat absorption.

The amount of fat in the form of soaps in the feces was neither proportional to the amount of calcium in the feces nor to the amount of the carbohydrate in the food.

Both the actual and percentage amounts of soaps were greater when the fat intake was low.

The nitrogen retention was greater than in normal infants of the same age and weight.

Increasing the amount of the carbohydrate produced an increased nitrogen retention, but the nitrogen retention was not influenced by the amount of fat in the food.

2033 Locust Street.

WARD PROBLEMS

FRANCIS HUBER, M.D.
Physician to Beth Israel Hospital (Children's Ward)
NEW YORK

The original ward for children at Beth Israel Hospital, located on the first floor, with a capacity of seventeen beds 2 feet apart, and 2 feet from the wall, cut down to thirteen beds to give the required air space, has been replaced by a new ward built on the roof. The number of beds has been increased so that at present we can accommodate about twenty-five medical cases in children up to the age of 10 years.

To digress a moment. Personally, I consider the presence of older children who are convalescent and able to be up and about, particularly girls from 6 to 8 years of age, to have a most beneficial effect on the younger patients. Not only do they hold the bottles, amuse and play with the little ones, when the condition of the latter permits: they at the same time act the part of volunteer "young mothers," for many of them are accustomed to mind their little brothers and sisters at home.

Our nurses are good and efficient, but their time is fully taken up with routine ward work. How much play means to the little ones in the absence of the mother I need not dwell on further or attempt to describe. To return to our subject.

Better provisions are also to be provided, thanks to the efforts of our efficient superintendent, Mr. L. J. Frank, and the broad views of our directors, for the surgical and otological cases.

Though the hospital is located in a thickly populated section of the "East Side," with unfavorable conditions around (a fish market to the northwest and a stable adjoining on the west) our results compare favorably with those of more pleasantly situated institutions.

In the new ward on the sixth floor, with a roof-garden above, we are singularly fortunate in the amount of sunlight, fresh air and freedom from street noise and dust. Situated about 55 feet above the street level, we have a clean sweep of fresh air circulating from the river, with extended and changing views, unobstructed by neighboring buildings. To the east of the ward there is an open space 12 by 26 feet not built up, affording a good view of the river, bridges, navy yard, etc., where the convalescing children may obtain the benefits of the open air. To the

north there is quite a space, protected and shady, available for similar purposes. The spaces referred to are used only by the children, ample provisions having been made by the hospital authorities some time ago for adults.

It is further contemplated, a little later on, to cover over the space to the east with a structure of angle iron and glass, so arranged as to have the sides open in summer and closed in inclement weather and winter. Our facilities, it is true, have been greatly increased, but there is still room for further improvement, particularly in line with a view to prevent or minimize the dangers of the occurrence of infectious diseases in the ward.

The problems that confront the "attending" in the management of a children's service are manifold and varied. Ideal conditions, demanding great outlay of money and space, possible in special hospitals, are almost impossible of realization in a general hospital with necessarily limited room and facilities. The exclusion of infectious diseases, as measles, scarlet fever and incipient whooping-cough, etc., with the longer or shorter period of incubation of the respective diseases, can only be accomplished by keeping new patients in a separate ward under observation for a period varying from one to two weeks or more.

This is not possible when a number of new cases present themselves in rapid succession. As long as we are not familiar with the specific organisms of a number of the infectious diseases there is danger of such cases being admitted in the very early stages before the characteristic symptoms develop. Recently an urgent case of empyema was sent in. Questioning elicited the fact that there was no scarlet fever in the patient's house. The child was operated. Four days later sudden vomiting occurred, temperature was noted, and the following morning a characteristic rash appeared.

As one or other of the contagious diseases is likely to crop out at almost any time in the thickly populated district, the house staff is always on the lookout. With the onset of any suspicious symptoms, the child is at once isolated and watched. We are particularly careful during the existence of an epidemic.

The early discovery and removal of suspected cases lessens the danger of a general ward infection. On three different occasions during the past two months we have been able to check a further outbreak by removing isolated cases of scarlet fever as soon as the rash appeared, not admitting new cases for a few days.

Children who have had scarlet fever or diphtheria, etc., may still carry the infection through the nasal or aural discharges. Careful histories of possible recent exposures or the presence of infectious cases in the family or neighbors should be elicited. It has occurred to us more than once that the family, aware of the fact that positive statements as to the presence of such diseases would exclude the patient, suppress such information. Sometimes the family physician is at fault, the family having been posted by him.

Before admission to the children's ward a careful examination is made of the nose, throat and skin. If nothing suspicious is detected, the patient is kept under observation for several days in a special room, until smears of the nose and throat and, in case of girls, vaginal smears have been made and the cultures reported negative. Routine examinations of patients in the ward are subsequently made at intervals, to discover possible bacilli carriers.

Diphtheria.—The type of the disease has changed materially. We do not, at the present time, encounter the severe cases so commonly met with twenty or twenty-five years ago. The improved hygienic and sanitary conditions and the methods adopted by the authorities have robbed it of much of its danger. With the precautions taken nowadays, earlier and more exact diagnosis and the advanced methods of treatment, the disease is more readily controlled and the mortality is less.

Visitors.—Visits to the ward by the family or friends ought to be interdicted. Aside from the danger of carrying in infectious diseases, there is the excitement, smuggling in of improper food or so-called dainties and interference with other patients, or the work of the ward. The effect of the visitors on the seriously ill patient is frequently detrimental. We are all familiar with the rise of temperature, restlessness, etc., following visiting hours. When the children's ward was located on the first floor, though the rule to exclude visitors was adopted, we soon discovered that it could not be enforced. The humor of the situation was evident when it was discovered that the fire-escapes were utilized by playmates and a bandage unrolled served as a string to smuggle in various articles while the nurses were engaged in their regular work. Since the service has been transferred to the roof, the rule has been more strictly adhered to. In exceptional cases of nursing infants, if the condition of the little one permits, the child is taken by one of the nurses to another room to be nursed, the mother wearing a clean gown provided by the hospital. If the child be too ill to be moved, the mother, in a clean

hospital gown, is permitted to nurse the baby in the ward. It is understood, of course, that proper supplementary feeding is carried on at regular intervals in these cases. The plan is on trial at present; perhaps it may work out favorably in practice.

Similar precautions are taken when patients are on the danger list. As the parents and friends are informed beforehand of these restrictions and the reasons therefor explained to them, but little trouble or serious objections have been raised. "Individual precautions" are strictly observed. The various articles are kept in white enameled tables with two drawers — one for each adjoining bed. Thanks to the liberality of Dr. A. Hymanson, "associate visiting" to the children's service, our facilities for this purpose have been greatly improved. Our obligations do not terminate with the discharge of the patient. Through the efficient cooperation of the social worker, convalescing patients, as soon as their condition permits, are sent to the country or seashore to recuperate.

Through the same source, we have in some cases been enabled to obtain the services of nursing women, to furnish a limited supply of mother's milk to some of our sick infants.

The social problem of dealing with marasmic or ill-nourished children and infants cannot be solved in institutions. The children can only be kept in the hospital during an acute exacerbation or because of some complication.

Better results are obtained by adopting Dr. H. D. Chapin's plan along the lines of family life practiced in the Speedwell Country Home Society.

To group pneumonia, diarrheal conditions, typhoids, etc., in individual wards, possible in an up-to-date children's ward hospital, is not feasible in a general hospital with a children's service. A proportionate number only should be admitted. There should be no overcrowding.

"Individual precautions," conscientiously carried out, lessen the dangers of ward infection. Again, I would say, chronic disturbances of nutrition in infants and young children, particularly during the summer, ought not to be treated in the institution, except to tide over an emergency.

The great increase in artificial feeding, the congestion of the population and the general conditions of existence have or exert a most depressing influence, in spite of better means of infant feeding. The stagnant air in the dwellings, the high temperature in rooms in summer with hot nights are factors of great moment in the causation of diarrheal affections.

Bacterial contamination of the milk, bacterial infection of the gastro-intestinal tract may be contributing causes, but they do not explain in themselves the high mortality during the hot months. Under the broad popular terms "summer complaint" and "summer diarrhea" are included the symptom-complex diarrhea, vomiting, fever, loss of appetite with more or less evident disturbance of nutrition. We have long recognized that the largest mortality occurs during the heated spell among children who have previously suffered from conditions of lowered vitality with digestive disturbances or whose digestion is below par. In private practice the removal of such children from the city to the country is advised as a therapeutic and prophylactic measure. We do not wait for the summer, but send them away late in the spring. Such too should be the rule in social work in the congested districts and in hospitals. Send such patients to the country, where the days and nights are comparatively comfortable and they will thrive, even if the milk-supply is not quite up to the standard.

Poliomyelitis and cerebrospinal meningitis have, during former epidemics, been allowed in the same ward with other children, without subsequent infection of other patients, many of them seriously ill and in lowered condition with such diseases as pneumonia, empyema, etc. Though the diseases referred to are undoubtedly contagious, the danger apparently is not great, for in our hospital experience no new cases have developed in the children's ward.

In spite of the differences as to the degree of contagiousness, general preventive measures are imperative and should not be neglected. The experiments of Osgood and Lewis strengthen the suspicion of human carriers and raise still further doubts as to the efficiency of prophylactic measures directed only to the persons in the acute stages.

The virus of poliomyelitis is destroyed by comparatively weak disinfectants, such as 1 to 500 potassium permanganate, 1 per cent. menthol in oil, a powder of menthol 0.5, salol 5, and boric acid 20. Frost[1] claims that a 1 per cent. solution of hydrogen peroxid destroys the virus and recommends the use of an antiseptic gargle of this remedy. It is important to remember that insects may be passive carriers of the infectious agent of this disease. Flexner and Clark have but recently demonstrated this danger in respect to contaminated flies. The American Orthopedic Association and the American Pediatric Society have issued a circular, which states that poliomyelitis may be communicated from one person to

1. Public Health Bulletin No. 44, Feb. 19, 1911.

another and by a third party. The cases should be strictly quarantined, the sputum, urine and feces disinfected, and the same rigid precautions adopted as in scarlet fever. It is further advised that public health authorities make a careful study of epidemics.

Bacilli Carriers.—The problem discussed under this caption is one of the utmost importance, presenting many difficult and obscure phases. As is well known, children ill with other diseases may reveal the presence of Klebs-Loeffler bacilli in the nose or throat, when the results of the usual routine cultures are obtained, without manifest clinical signs.

The danger to others and our therapeutic helplessness in getting rid of the bacilli, in these cases, is evident to all. Local treatment appears to have little or no influence in causing a disappearance of the organisms. Sprays of various antiseptics have been tried. Irrigations with different solutions give negative results. Ointments appear to offer a certain degree of protection by coating the nasal mucous membrane. I have been particularly pleased with a weak calomel ointment.

Prevention from contact is most important. Experience has taught us further that the infections may be transmitted from one bed to another by "the spray of the open cough and the open sneeze."

Northrup advises a "grille" or bed screen, consisting of a three-leaf wire screen with two-way hinges.

Holt, with increased facilities and room space, adopts a better plan in resorting to the alcove arrangement, marble or heavy plate-glass slabs serving as partitions between the beds.

Antitoxin is of no avail in "carriers," even in large doses. Perhaps local treatment along the following lines may solve the difficulty.

An editorial[2] refers briefly to experiments made by several Russian physicians.

Dserhovsky produced an active immunity by introducing subcutaneously rising doses of diphtheria toxin. He also demonstrated on himself that the toxin may be introduced in the simplest way, by passing into the nostrils for several days in succession pledgets of cotton soaked in the toxin. The degree of active immunity by this method is greater, though it takes a longer time to develop.

Notwithstanding the preliminary routine examination and the negative bacterial findings in the vaginal smears, a more or less abundant discharge is occasionally discovered some time after admission.

---

2. Med. Rec., New York, May 6, 1911.

Though the characteristic organisms are now discovered for the first time, the case is not necessarily a new infection — it may be merely a recrudescence of a latent infection, to be isolated without delay. In hospital practice the slightest discharge should be investigated. It is an excellent plan to place a small piece of sterile gauze against the labia in order that any excess of secretion may be detected early. In our children's service, when a case is detected, the little patient is isolated at once or transferred to the female medical ward where the danger of spreading the infection appears to be *nil*.

No matter what measures are taken, though the nurses may be under special instructions and specific precautions observed, specific vulvovaginal catarrh is ever a source of danger in a ward. There is the danger of a weak link in the chain; the only way to prevent a ward infection is to remove and quarantine the affected patient. The cases are highly contagious and the epidemics difficult to control.

An exhaustive study of the subject, extending over a number of years, was instituted by Holt. I cannot express too highly my appreciation of the work done by him. I indorse most fully his conclusions, having had ample opportunities to study the subject in hospital, dispensary and private practice. I shall take the liberty to quote the following from his article, "Gonococcus Infections." [3]

"In a disease so difficult to cure and so highly contagious, the utmost importance must be attached to measures of prevention. In the light of our experience two things are essential in institution practice: first, cases of gonococcus vaginitis must so far as possible be excluded. In the second place, if admitted by accident or otherwise they must be quarantined. In excluding cases only one thing can be depended on, viz., microscopic examinations of a smear from the vaginal secretion before the child is received."

In the paper on vulvovaginal catarrh,[4] the writer asserts: In institutions it may spread rapidly and appear epidemic in character. It is a good plan under such circumstances to isolate the cases. Additional nurses should be assigned and their entire attention devoted to the little patients. During the existence of the trouble strict isolation should be insisted on, the patients quarantined until the microscope fails to reveal the infectious organisms.

3. New York Med. Jour., March 18 and 25, 1905.
4. Arch. Ped., Dec. 1, 1899, viii, 480.

On page 482, under Treatment, the statement is made that "the patients should be isolated and quarantined to prevent the spread of the infection. The necessity of a strict adherence to this rule is evident to anyone who has had experience in this line."

The relatively frequent occurrence of colon bacillus infection of the urinary tract, at least 90 per cent. of the cases occurring in female infants, requires careful study with a view to prevention. In a large proportion of the cases, the process is supposed to be due to the ascending infection from without — contamination from the rectum.

The close proximity of the urethra to the anus, the short urethra of the female, and the frequent contact with the discharges, together with the habit of working with the diaper from behind forward, lends a very plausible explanation to this view.

The treatment of chorea, excluding the rheumatic type, presents some interesting features, in view of the neuropathic condition of many of our patients. There is the possible danger of the development of new cases in neurotic children through mimicry or mental impressions on an unstable nervous system. The severe cases are kept in cribs, the sides being high, well padded and covered, thus forming an efficient screen. Kept under the influence of codeia, warm baths being given daily, the patients do far better in the ward than if isolated. Thoughtless and mischievous as children are, I have frequently been surprised by the consideration shown the afflicted patients by their companions in the ward.

The not infrequent occurrence of a number of cases of otitis in the ward in patients suffering from various affections deserves further study with a view to prevent such outbreaks. Now and then, particularly when a number of typhoids, pneumonias or empyemas have been in the ward for a time, the patients develop an acute nasal catarrh, with negative bacteriologic findings, yielding readily to normal saline douching. A little extra attention to the toilet of the nasopharynx may abort such mild epidemics in children predisposed to catarrhal conditions in consequence of the presence of lymphoid hypertrophies.

The dangers of "hospitalism" are greater in the infant and young child. Patients under 2 years ought not to be allowed to remain any longer than absolutely necessary after convalescence has been established. The older the child, the less the danger.

The reprehensible practice of cleansing the mouth of little patients with gauze or absorbent cotton wrapped about the little finger should be abolished. Bednar's aphthæ in the infant and a possible infection or

spreading of disease through bacilli carriers are a few of the dangers. Small swabs, made with wooden tooth-picks and absorbent cotton, are preferable.

The frequent administration of a weak acidulated drink or frequently moistening the lips with a solution of borax 1 dram, glycerin one-half ounce and rose water 4 ounces, serves the purpose of keeping the lips, gums and mouth in a fair condition.

The above is not an exhaustive exposition of the subject; it is merely suggestive and written in the hope that it may bring out the views of our members and the precautions taken by them in their hospital practice.

THE RECURRENCE OF SCARLET FEVER, WITH REPORT OF A CASE

J. P. CROZER GRIFFITH
Clinical Professor of the Diseases of Children in the University of Pennsylvania.
PHILADELPHIA

That certain infectious diseases may occur more than once in the same individual is a well-known fact, the incidence depending somewhat on the nature of the malady. Thus, influenza offers apparently no protective power against subsequent attacks, and, indeed, rather predisposes to them, and immunity from a second attack of diphtheria appears to be but temporary in many individuals. Pertussis, rarely repeating itself during childhood, is not so infrequently seen developing a second time after adult life is reached. With measles and scarlet fever, however, the case is very different. One often hears the assertion made by some of the laity that they have had measles two or three times. Most of these statements are certainly incorrect. In view of the existence of rubella, which often simulates measles very closely, and the occurrence at times of morbilliform erythemata from various sources, the possible source of the error is evident. Indeed, the observations of Maeselis[1] indicate that second attacks of measles are even less common than second attacks of scarlet fever, and this is the opinion shared by many pediatrists. Since the discovery of the buccal eruption, the occurrence of second attacks of measles is less frequently reported, although it is to be noted that this eruption may occasionally occur in rubella as well.

It is, however, with the recurrence of scarlet fever that we have to do. This recurrence in the typical form is certainly of the greatest rarity. I am not, of course, referring to the attacks of sore throat from which those in attendance on scarlet fever sometimes suffer. As with measles, one hears from the laity of second attacks of scarlet fever experienced, and even physicians speak of them. In the great majority of cases, however, the physician who has seen the second attack has to take the occurrence of the first on hearsay. Even in the instances where a physician thinks he has seen two or more attacks in one person, he must not forget the very great similarity which many cases of scarlatiniform rubella bears to

1. Virchow's Arch., cxxxvii, 468, 1894.

scarlet fever, and the existence, too, of such conditions as scarlatiniform erythema, and acute desquamative dermatitis, the latter being capable of simulating the eruption of scarlet fever exactly, even to the desquamation of large flakes or, possibly, cutaneous casts. Diphtheria with erythema has frequently been mistaken for second attacks of scarlet fever.

That the recurrence of scarlatina is rare is supported by the testimony of most pediatric writers. Consultation of a few text-books at hand resulted as follows;

Thomas,[2] although citing reported instances from medical literature, has himself seen it but once in hundreds of cases; Henoch has seen it only once; Moizard[3] warns against the great danger of mistakes in making the diagnosis of a second attack; Holt speaks of recurrence as very exceptional; Gerhardt and Seifert describe it as remarkably rare; Schick[4] reports a single case; Bohn[5] describes it as rare; Baginsky reports recurrence in two patients. Only Heubner has seen it more frequently — six times in 358 cases, and in two of these the disease was represented merely by severe sore throat. Koplik, also, has seen second attacks.

Journal literature contains a number of scattered references to recurrence of the disease. Thus Körner[6] cites a number of cases from medical literature. Yasny[7] reports an individual with three successive attacks at comparatively short intervals, and Kurson[8] a similar case with three typical attacks at intervals of a year. Dunckel[9] saw recurrence after one year, and Widowitz[10] in 323 cases of scarlet fever observed recurrence twice, both instances apparently beyond doubt. Weissenberg,[11] although showing that writers in general find recurrence rare, reports seven cases seen by himself, and quotes Trojomowsky who asserted to have seen it eighteen times in 300 cases. This list of references might be readily extended.

That one infectious disease may occasionally be combined with another is, of course, generally recognized. Diphtheria very frequently complicates scarlet fever or measles, and pertussis and tuberculosis are often

2. Ziemssen's Handbuch.
3. Grancher and Comby: Traité des maladies de l'enfance.
4. Pfaundler and Schlossmann's Handbuch der Kinderheilkunde.
5. Gerhardt's Handbuch der Kinderkrankheiten.
6. Jahrb. f. Kinderh., 1876, ix, 362,
7. Abstracted in Rev. mens. des mal. de l'enf., May, 1904.
8. Abstracted in Brit. Jour. Child. Dis., 1909, vi, 233.
9. Arch. Pediat., 1904, xxi, 30.
10. Wien. klin. Wchnschr., 1909, xxii, 1596.
11. Jahrb. f. Kinderh., 1909, lii, 17.

associated as mutually complicating or following each other or measles. Other combinations are often seen, the occurrence of which in the experience of any one observer, however, is generally uncommon enough to make it a matter of interest. I have seen, for instance, the association of typhoid fever with scarlet fever, typhoid fever with measles, typhoid fever with varicella, typhoid fever with cerebrospinal fever, typhoid fever with rubella, measles with varicella, measles with varicella and diphtheria, and measles with scarlet fever. Several instances of the latter have been under my care. I merely refer to these combinations in passing because, although the following case is reported to illustrate the recurrence of scarlet fever, it exhibited also in one of the attacks the combination of measles with this disease. The case history is as follows:

J. C. A., aged 2 years, the child of a physician, was attacked April 12, 1900, with nose bleed and vomiting. On the morning of the 13th he did not appear to be ill, but in the afternoon he vomited again. On the afternoon of the 14th I found a typical scarlatinal rash on the thorax and abdomen. The patient had the ordinary course of mild scarlet fever, the appearance of the tongue and of the throat being entirely characteristic of this disease. The efflorescence disappeared entirely during the first week, but on the 20th, a week from the first evidence of illness, he commenced to sneeze and the next day to suffer from cough and lacrymation with a temperature of 103 F., and on the 23d, the fourth day of catarrhal symptoms and the twelfth day of the attack of scarlatina, a typical eruption of measles developed. The child apparently suffered more from the measles than from the scarlet fever and exhibited a higher temperature. The desquamation of measles was apparently replaced, or at least concealed, by a typical desquamation of scarlet fever, the skin coming off in large pieces. Otitis media followed.

The child remained entirely well until May 14, 1901, thirteen months later, when he became restless and feverish during the night, and in twenty-four hours was covered with a typical scarlatinal eruption. I made the diagnosis immediately of scarlet fever, forgetting that there had been a previous attack. This fact would, naturally, have thrown doubt upon the diagnosis were it not that the tongue became again typically scarlatinal, there was a characteristic sore throat, and desquamation finally occurred. This latter was in the form of large plaques upon the hands and feet. A little over two weeks from the onset a postscarlatinal nephritis developed.

There seems to me to be no reasonable doubt regarding the occurence of two distinct attacks of scarlet fever in this patient. The diagnosis in neither was based upon the eruption alone, but upon the complex of symptoms characteristic of the disease.

1810 Spruce Street.

DUODENAL ULCER

J. P. CROZER GRIFFITH, M.D.
Clinical Professor of the Diseases of Children in the University of Pennsylvania.
PHILADELPHIA

Duodenal ulcer occurring in early life is a condition which appears to be so rare or so little considered that the majority of text-books take no note of it whatever. In the various works at hand which I have briefly consulted, the only reference I have so far found is in the article by Fischl,[1] in which gastric ulcer in early life is spoken of as extremely rare and duodenal ulcer as even less frequent. Journal and special literature, it is true, give somewhat fuller notice of it. Among these references may be mentioned the cases of Simmons,[2] in two children of 8 years and of 4 years, respectively; Borland,[3] in an infant of 8 months; Torday,[4] in an infant of 8 months; Sochaczewski,[5] in two infants, of 5 and 4 months, respectively; Freund,[6] in an infant in the last quarter of the first year; Kuttner,[7] in a child of 4 years; Hamen,[8] in a boy of 10 years; Krannhals,[9] in a boy of 5 years; Finny,[10] in an infant of 2½ months, in whom the lesion was associated with pyloric stenosis; and Adriance,[11] in an infant of 10 months. Only Collin,[12] among writers, appears to consider the disease comparatively common in childhood, finding in 279 reported cases forty-two under 10 years of age. Of these, however, seventeen, i. e., almost half, occurred in the first year of life, and possibly many of them at the time when melena neonatorum may have been present.

Duodenal ulcer is indeed undoubtedly a cause of melena neonatorum, the majority of cases of ulcer belonging to this period; and Moynihan[13]

1. Pfaundler and Schlossmann's Handbuch der Kinderheilkunde,, ii, 1, 141.
2. München. med. Wchnschr., 1898, xlv, 434.
3. Lancet, London, 1903, ii, 1084.
4. Jahrb. f. Kinderh., 1906, lxiii, 563.
5. Archiv. für Kinderheilkunde, 1909, l, 25.
6. Mitt. a. d. Grenzgeb. d. Med. u. Chir., xi, 326.
7. Berl. klin. Wchnschr., 1908, xlv, 2009.
8. Medical News, 1891, lix, 131.
9. St. Petersburger med. Wchnschr., 1891, xvi, 327.
10. Proc. Royal Soc. Med., 1908-1909; Section for diseases of children, p. 67.
11. Arch. of Pediat., 1901, xviii, 277.
12. Thèse de Paris, 1890.
13. Duodenal Ulcer, 1910, 89.

has quoted from medical literature sixteen cases of melena in the first week of life in which duodenal ulcer was found at autopsy. Ulcer is also discovered occasionally in atrophic infants later in the first year, and Helmholtz[14] reports nine instances occurring under these circumstances.

The list of reported cases could be extended, but enough has been said to show the rarity of the condition in early life. In fact, in 186 cases operated on by Moynihan,[13] the youngest was 17 years of age. The following two cases are therefore not without interest — the first one, necessarily somewhat uncertain; the second proved by autopsy.

John L., aged 10 years, had been previously in good health except for a tendency to coating of the tongue and occasional constipation. A few years before he had suffered from scarlet fever with a postscarlatinal nephritis, which lasted for a number of months. Toward the end of January, 1909, he ate some indigestible food. This was followed by vomiting for which the mother gave calomel and a saline. Recovery followed promptly. On February 7 he was exercising upon a trapeze and the parents seemed inclined to associate with this fact the condition which followed, but there was no distinct history of any unusual pressure brought to bear upon the abdomen at this time. When at school on the morning of February 8, he was seized with dizziness and faintness and could hardly walk home, and in the afternoon he vomited his dinner. He again attended school on the following day, the 9th, but felt tired and vomited in the afternoon, and a purgative was given. Later in the afternoon of this day he had several loose, bloody movements, of a distinctly red color, without pain. On February 10, he was pale, nauseated, but had no fever, and passed several more liquid, bloody stools. The evacuation of blood continued for several days, the movements growing constantly darker, and the evidence of blood not disappearing entirely for a week or more. Meanwhile pallor increased with faintness if the child raised himself to a sitting position. The hemoglobin percentage fell to seventy and that of the red blood corpuscles to somewhat over 2,000,000; there was slight abdominal distention, but no pain or tenderness discoverable. The boy was seen with me repeatedly by Dr. J. H. Musser, who concurred in the diagnosis of a probable duodenal ulcer. The diet was very carefully regulated and subsequently cautiously increased, while rest in bed was enforced. Improvement in general health and in the anemic condition was slow but steady and convalescence seemed complete early in May, about three months after the onset, except for slight irregularity of the heart's action following exercise, and a faint hemic murmur.

On Sept. 19, 1910, the child possibly subjected himself to an unusual strain in making a backward dive into the swimming pool. On the 20th he was pale, and on the 21st he had a somewhat dark stool. On the 22d, a formed, absolutely black stool was passed, which examination showed to be due to the presence of blood. Dark bowel movements continued for from one to two weeks; the hemoglobin meanwhile fell to 70 per cent., but the general condition kept good. Up to the present time (May, 1911) there has been no return of the symptoms.

In the fortunate absence of a fatal ending the diagnosis could not be confirmed by autopsy, and must necessarily remain uncertain. That of

14. Deutsche med. Wchnschr., 1909, xxxv, 534.

duodenal ulcer was made largely by exclusion, there being no reason to believe in the existence of any tuberculous lesions lower in the bowel, no evidence of colitis, and no hematemesis, such as would have appeared in gastric ulcer. The presence of hematemesis would not, of course, have contra-indicated the existence of an ulcer in the duodenum.

The following case is a certain instance of the disease:

Edward K., aged six months, was seen by me on January 31, 1910, in consultation with Dr. Theodore Sprissler, whose connection with the case dated only from the preceding day. The child had been fed artificially in various ways after the fourth week, but had suffered constantly from gastrointestinal disturbance and failure to gain in weight. Weaning was complete at the age of six weeks. After this time constipation developed with the passage of very hard stools, and for the treatment of this condition the physician then in attendance ordered a milk mixture rich in fat. This apparently resulted in vomiting, which continued to be a troublesome symptom to a greater or less extent in spite of many changes in the method of feeding. At times the infant appeared to be in great pain, and later, as when seen by Dr. Sprissler, he was able to retain food only when given a few teaspoonfuls at a time. Finally on the evening of January 30 he exhibited a streak of blood in the vomited matter, and passed a dark stool, probably blood. On the morning of the 31st, at about 9 a. m., he vomited about a half ounce of liquid blood which contained a rather large sized firm clot, partially decolorized. He passed promptly into a condition of profound collapse, being apparently moribund when seen again by Dr. Sprissler at 11 a. m. He had revived remarkably when seen by me at 2:30 p. m., at which time examination showed a moderate degree of emaciation with fairly good circulation and a strong cry. The infant was entered in the Children's Medical Ward of the Hospital of the University of Pennsylvania, but during the night again vomited blood, this time in considerable amount, had a large hemorrhage from the bowel and passed into collapse. A subcutaneous injection of gelatin was given but without benefit, and the infant died early on the morning of the next day, February 1.

The autopsy made by Dr. B. S. Veeder showed an ulcer about two millimeters below the pylorus in the superior horizontal part of the duodenum on the posterior wall. It was rounded and had a punched out appearance with smooth edges, was about five millimeters in diameter, and extended through all the layers of the bowel. Adhesions externally had prevented the escape of fluid into the peritoneal cavity. There was no stenosis of the pylorus present, and no other alteration of the intestine except the staining of the mucous membrane due to a large amount of hemorrhagic fluid. The stomach contained about thirty cubic centimeters of thick, dark reddish material. There were present also the lesions of an acute hemorrhagic nephritis, circumlobular fibrosis of the liver with parenchymatous degeneration, and moderate medullary fibrosis of the adrenals.

1810 Spruce Street.

WARD IMPROVEMENTS; CRIB WARMER; MANAGEMENT OF "CARRIERS"; PREVENTION OF EPIDEMICS; CHILDREN'S SERVICE, PRESBYTERIAN HOSPITAL

W. P. NORTHRUP, M.D.
NEW YORK

How may we avoid receiving into a ward not only cases just developing communicable diseases, but how protect the wards from cases exposed and not yet showing symptoms, how, in short, may we strain out from the inflowing current of applicants and emergency cases those individuals who within a few days may disseminate the germs of an epidemic? Granted that we are not at present very hopeful of complete success, it remains to consider how we may improve our methods to the end that we may keep the children's wards out of quarantine more and more.

At the Presbyterian Hospital we have had the service closed time and time again by measles and other communicable diseases. We have had the usual experience with vaginitis, diphtheria-carriers, and desquamation of unknown origin. From these experiences we have learned something.

Entrance Examination.—There are several ways of entrance to the service — by examination at the front door by an intern deputed for the week; by the dispensary physician, children's class, each case approved by the house physician; and by an ambulance in emergency service. Emergency cases requiring immediate hospital attention, such as operation, are received and taken care of whatever associated germs they may carry. As a last resort there is always the isolation pavilion. By the regulations here described we have increased the efficiency of the service, allowing the wards to run fuller and diminishing quarantine closures.

FRONT DOOR EXAMINATION OF APPLICANTS

The examination room is provided with the usual facilities of examination, including culture tubes, plus this card, which explains itself:

ADMISSION CARD
(CHILDREN)

Name .....Age .....
Address .....
What contagious diseases has the child had?
.....

What contagious diseases are prevailing in the child's immediate family and vicinity?
(For further information call Col. 4900, Contagious Disease Dept., Department of Health.)
.....
.....
Does the child present any evidence of contagious disease?
.....
.....
.....
Examining Physician.
Date.....19
48-3M-59 [OVER]

In order to stimulate the memory of the routine examiner, he is asked to refer to the other side of the card and also to sign his name. This card accompanies the history until the patient is discharged.

[REVERSE]

No contagious diseases are admitted to the hospital.
Patients free of contagious disease are admitted to the Observation Ward.
Patients so seriously injured or so seriously sick as to require admission to the Hospital in order to save life, even if complicated by a contagious disease, may on application to the Superintendent be admitted to the Isolation Pavilion.
The most common contagious diseases to be guarded against are:
In reporting use numbers.

Diphtheria	"No. 1	Dept.	of	Health"	
Scarlet Fever	"No. 2	"	"	"	
Measles	"No. 3	"	"	"	
Small-Pox	"No. 4	"	"	"	

Vulvovaginitis
Whooping-Cough
Ringworm
Trachoma
Mumps

This method of observation serves very well in deliberate work. The mishaps arise from the ambulance cases, automobile accidents, for instance, when no delay is possible. These cases are detained in the accident ward till morning when feasible, or in some detention room awaiting a daylight examination, and are then sent to the observation ward with other entering cases.

Observation Ward.—All cases entering the children's service are detained here until the head physician of the ward is satisfied that no infectious disease is threatening. The ward consists of a main large room, two isolating rooms, and the necessary service rooms. The capacity is four beds, with the possibility of adding four more. The cases remain in this ward until passed on by myself. It is impossible to divide the responsibility; one person visiting the ward every day must assume such responsibility. Cultures are made from the nose and throat, and vagina smears are examined before the case is considered eligible for moving up into the ward. Of course the mucous and skin surfaces are most carefully examined in good daylight. The length of sojourn in the observation

ward depends on the verdict of the responsible visiting physician. A boy suffering from pneumonia may be hurried through to the roof ward, while a girl without urgent symptoms may remain three days. Our cases are inspected in the morning in good daylight. I assume that with this audience it is unnecessary to dwell on the details of individual precautions. Suffice it to say that we have separate enameled tables, containing individual necessities for each child — a complete outfit. The necessities for bathing are contained in this table — no tubbing is allowed. After removing to the main ward the same individual precautions are preserved, the bathing now being done in the washing room, to be later describ

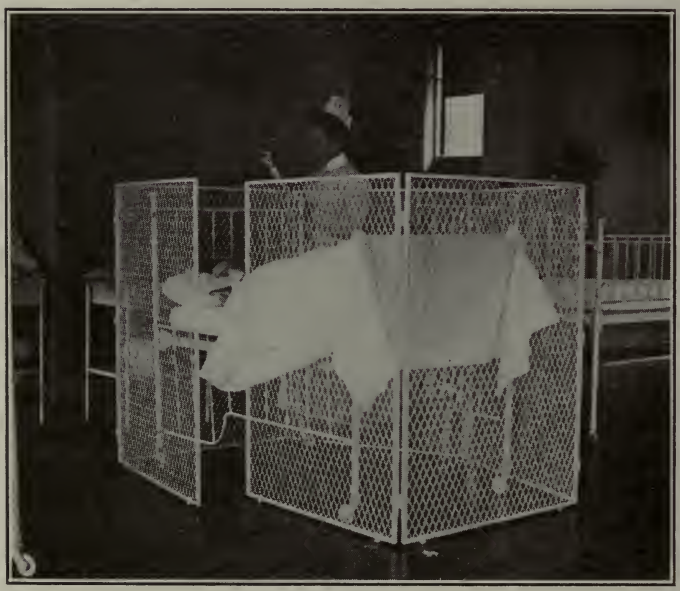


Fig. 1.—Bed screen

Figure 1 depicts a bed screen or "grille." This is designed to isolate within the ward "suspects," and all newly arrived patients are suspects.

We believe that, with few exceptions, diseases are communicated by contact or near approach of "carriers." The unexplained outcropping of contagious diseases is due to carriers, who do not suffer from the disease themselves and are not therefore suspected. The bed screens are placed around typhoid, influenza, bronchitis, bronchopneumonia, whooping-cough, chicken-pox patients and "carriers" of diphtheria bacilli. With

the space, the air currents, the personnel of nurses and interns which we now have, I believe the experiment is justified.

I wish to say that Dr. H. M. Biggs has personally visited the service and shared the responsibility of this experiment in the capacity of adviser and consultant.

After a whole winter's experience without accident and after all the cases are well and restored to their homes, I feel that I may report the bare facts.

The screen keeps the children, the runabouts, from visiting within the carrying radius of coughing and sneezing — 3 to 5 feet. Transmission of disease germs is nearly always immediately from one warm, moist mucous surface to another, and rarely by quick mediate transmission ("fomites"). A screen sufficiently large to surround a bed consists of two units of three leaves each. Each leaf is 4 feet high, 3 feet wide and swung on two-way hinges. In the most approved, latest screens the hinges are mounted on an upright standard after the manner of the usual fire screen. This mounting is strong, does not "wabble" — the upright bears the weight of the screens.

An ambulance case of empyema, appendicitis, or automobile accident, incidentally a carrier of diphtheria bacilli or gonococci, cannot be transferred to special hospitals without suffering from the lack of surgical treatment. We do not contend that there is no danger from the bacilli in the nose, but with a properly trained personnel and with the isolation which the screen affords, they can be safely treated in the ward. Immunizing doses of diphtheria antitoxin are usually administered to "runabout" children.

In this connection I wish to refer the reader to a recent publication of Dr. Alvah H. Doty, Quarantine Commissioner, "Prevention of Infectious Diseases." The fallacy of certain theories regarding the transmission of infectious diseases is here shown, and Dr. Doty's vast personal experience has corroborated the views here set down.

The illustrations show the essentials of construction. The screen units can be linked together indefinitely and sufficiently to surround an adult ward bed. We have found the screen an aid in keeping visitors from kissing patients to their entire satisfaction. No amount of rules or screens will keep mothers from kissing their babies in their mouths, but altogether we have had but one case of measles in the service during this winter's extensive epidemic and no second case from the one. We allow

the nearest of kin to visit on regular visiting days. The ward has not been thrown out of function in three years.

The old-time tub has been discarded. In its place we have adopted the spray bath. Babies can be bathed in less than half the time, more comfortably to the nurse, and as for the baby, more agreeably and with vastly less danger from communicated infection and from burning by hot water.

The wards of the Presbyterian Hospital are usually cool, 60 to 65 F. in winter, and the bath-room must be comfortable, usually 70 to 75 F.

Fig. 2.—Bed screen

This room, which we call the "grooming" room, is thoroughly heated, so that every surface, every fabric, the slab and water are all agreeably warm. The facilities offered in order to make this method popular must please everybody and be safe. Such it has proved, and no accident of burning has occurred, and it seems to be "fool proof."

The results of experience for three years justify us in assuring those interested that the danger of infection is greatly reduced. We have not known of any transmission. The infants are practically bathed in a running stream. Nothing is used a second time, except the bath towels in which the child lies. They are immediately thrown into boiling water.

to be used once more on another day. This is to economize laundry work. The soap is liquid and shaken from a bottle, the powder is shaken from a box, the gauze wash rags are burned, towels are immediately boiled.

To fill a bathtub, secure the correct temperature, bathe the baby, empty the tub, clean it, disinfect it, refill it and secure the proper temperature requires time and a conscientious worker.

Fig. 3.—Bathing of babies

CHILDREN'S SERVICE

DAILY REPORT TO THE ATTENDING PHYSICIAN OF WARD REGARDING INFECTIOUS DISEASES

1. MEASLES—Skin eruptions, catarrhal symptoms, Koplik spots?
2. VULVOVAGINITIS—Discharge, pus, redness, gluing together of labia, micro-organism found?
3. DIPHTHERIA—Exudate, nasal discharge, bacilli found?
4. SCARLET FEVER—Skin eruptions, marked redness of throat, desquamation?
5. OTHER CONTAGIOUS DISEASES?

Are there any evidences of contagious diseases in the Wards?

Yes. No. .....
House Physician.

Yes. No. .....
House Surgeon, Div.

Yes. No. .....
House Surgeon, Div.

REMARKS—If there are evidences of contagious disease, mention the facts and the temporary disposal of the case.

Date.....19

Description of Bath Facilities.[1]—Beginning above, one sees an 80-gallon tank; the water heated at will, usually to 103 F. The temperature is read off on the thermometer projecting from the left of the lower quarter. This tank is filled by the same nurse each day, the temperature noted by the head nurse and the hot and cold intake pipes shut off till further orders. This insures a constant temperature (103 F.) in the tank and about 100 F. as it runs from the spray. The water gauge shows on the face of the tank. In this glass tube the amount of water in the

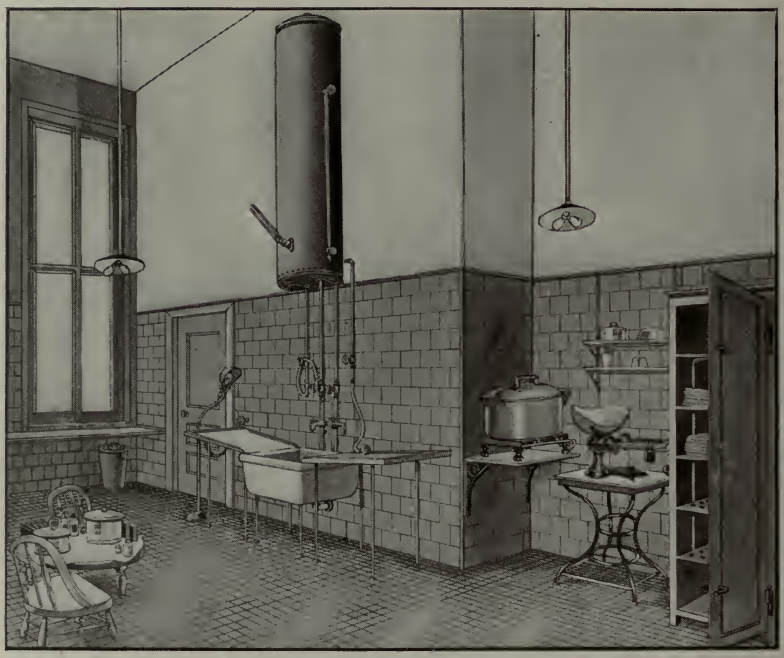


Fig. 4.—Bathing apparatus

reservoir can be easily noted. Mixing the hot and cold water is effected as follows: The hot and cold water pipes are turned on together while the filling and temperature are noted by the nurse deputized for this purpose. The hot and cold water pipes within the tank terminate in four points somewhat like a miniature gas-fixture, the hot-water tips pointing downward, the cold-water pipes pointing upward. The current of the two streams goes against their gravity tendency and so interdigitates that a

1. Medical Record, May 8, 1909.

thorough intermingling of currents is effected, and there can be no layers of hot and cold water. The contained water is of uniform temperature throughout. Eight gallons is found to be enough to serve for a morning's work. There are overflow pipes.

Below the tank are seen two flexible rubber pipes terminating in the usual metal bath-spray tips. From these it is designed that the water shall flow at 100 F. uniformly during the entire morning's work.

On the next lower level is seen a sink winged with two sloping marble slabs. These slabs are warm and on them are laid individual bath towels and the baby. After each bath the towels are boiled.

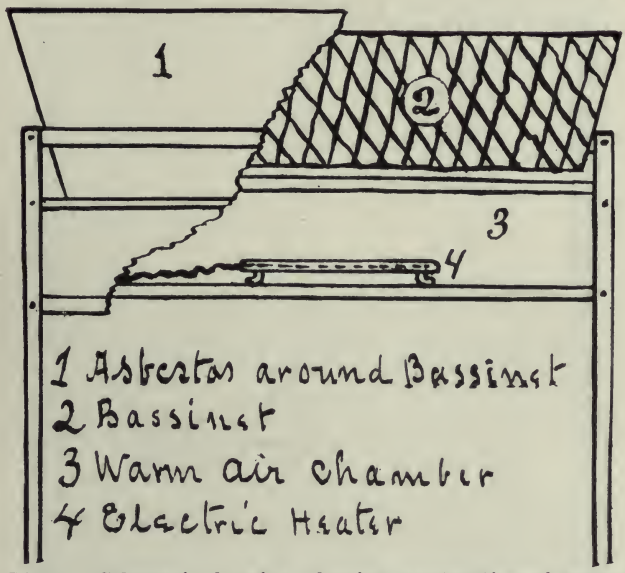


Fig. 5.—Schematic drawing, showing construction of warmer

To the extreme right is seen the hot closet from which the fresh clothing is taken dry and hot.

At the extreme left are seen the low nursery tables and chairs found convenient in dressing the children.

It is noted that a very large window lets in a flood of light, so that the slightest eruption or change of color or abnormal appearance of the mouth, tongue or eyes can be easily detected. An electric reflector in addition to the overhead lights serves the same purpose at night. There are two doors, one leading to the corridor and one (that shown in the illustration) to the toilet.

Result.—After several months' use, the apparatus and general facilities of the room have proved satisfactory.

1. The babies are washed in less than half the usual time.

2. The babies seem to be more comfortable and happier during bathing. They seem thoroughly to enjoy the warm room and warm spray; they wriggle and gurgle and crow.

3. Danger of infection from promiscuous tubbing is avoided.

4. Mishaps from the use of over-hot water are thus far avoided, and it would seem that the chances are reduced to the minimum. As a general

Fig. 6.—Crib Warmer or Incubator. A corner of the Children's Ward, showing (in the foreground) an especially devised crib. It is constructed of asbestos board and contains in a lower compartment an electric heater of the right heating capacity to keep the mattress warm for feeble and low-conditioned babies.

proposition one is painfully conscious that it is always possible for novitiates, excited individuals, mothers and doctors as well as nurses, to have mishaps, with unfortunate results, in the combination of baby and hot-water baths.

Results.—No new infections. No burns.

A baby with cold feet cannot digest, and a poorly nourished baby must have artificial heat until it can furnish its own. Hot-water bottles are expensive, troublesome and perilous. In using many hot bottles for an extended time accidents of burning are sure to occur. The apparatus here shown is believed to meet all the demands, correct all the faults and avoid all the perils here mentioned.

The electric crib warmer consists of a shallow asbestos box containing an electric heater; above this an abestos trough in which rests the usual ward bassinet. Our first heater was made by the engineer from material he had "in the house," an ordinary electric foot warmer, asbestos boards, cable couplings and switch which allow the current to be regulated to "high," "low," "medium" and "off." This primitive beginning has been somewhat improved, though the first one worked satisfactorily. It is desirable to have above the heater and within the box a diaphragm of metal or asbestos to produce a circulation. The diaphragm should be complete from side to side, but not reach to either end of the box. It should be tilted up toward the foot-end, so that the heat may rise up along the under side of the inclined plane of diaphragm, around the end at the foot of the crib, slide down again along the upper side to the interval at the head-end of the crib, and so on around the circuit. Circulation is an advantage to the distribution of heat and to the preservation of the electrical apparatus itself. Any engineer can copy this at pleasure; the cost of material is about $14. A manufacturing firm has planned to put a heater on the market, but it has not, to my knowledge, appeared, and there is no patent.

After a whole winter's almost constant use of six electric crib-warmers of the type described, we may report results satisfactory. No accident of any kind has occurred. It is impossible to burn a baby. It is easy to regulate the heat to the desired degree, varying it from hour to hour, also turning it off at will. We have kept the six warmers going all day and all night in cold weather, varying the heat as needed. It is readily seen that it is very little trouble to manage; it costs less than water bags in money and trouble. The electricity sufficient for an ordinary 16 C. P. illuminating bulb is all that is required.

As an incubator for premature babies it would seem to meet all indications. Heat comes up from below, the baby lies low in the bassinet, the sides of the asbestos trough come higher than the bassinet, so that the baby breathes warm air which circulates freely.

The electric crib-warmer saves trouble, cost in water bags, danger from burning, and does keep the baby comfortable in cold weather.

HOSPITALS FOR THE CARE OF INFANTS AND CHILDREN, AND THE METHODS OF PREVENTION OF INFECTION

HENRY KOPLIK, M.D.
NEW YORK

One of the most interesting questions concerning the hospital care of infants and children is that of the prevention of infections. Infections sometimes insignificant at first may subsequently lead to the death of the individual. We know that the age is of great moment in considering this question. Mild infections at birth or in early infancy receive much greater consideration at the hands of those to whose care we look for the avoidance of these accidents, than at a later period of life.

In hospitals which house infants and children the question of the separation of the infants of tender age from older children is an important one for various reasons, the chief one being that the attention is centered more intently on the care of the infant in a service which is devoted exclusively to their care than in one in which infants and older children are grouped in the same ward. In certain institutions, such as those of Keller in Berlin, the Augusta Victoria Haus, the whole hospital is devoted to the care not only of premature infants but of infants under a year or 2 years of age. I mention this institution of Professor Keller, because it is of most recent construction, best equipped, and probably the finest institution in the world devoted exclusively to the care of infants below the age of 2 years.

Of other institutions, similar in nature but not at all to be compared to it in perfection of detail, is that of Finkelstein in Berlin. It is not as modern in construction. It is a species of asylum or house in which infants supposedly orphans are received; they are kept in it a short time and then discharged into care outside the institution. These are two institutions, so-called asylums, devoted to the care and bringing up of young infants and nurslings. They may fairly be compared, the one most recent and the other institution of not so recent date.

In the one institution, that of Keller, every detail known to modern science in the care of premature and young infants has been drawn on to make the uniform whole. The wards are bright, the light streams into them, and seems to come from all sides. The cribs are far apart, the

clothing and linen immaculate and the little charges look well. The ventilation is perfect; no odor of any kind is perceptible when one comes into the ward. The nursing personnel is of the higher type. In this institution infections are rare. In two years they have had only one case of vaginitis, and this came into the house. Furunculosis is also extremely uncommon. There has been only one epidemic, if it can so be called, of pertussis; that is, three or four prematures developed a pertussis-like cough, and this infection was quickly controlled. I saw no infants with hideous or infectious ulcerations which had developed in the house. The whole tone of the ward was that of cleanliness, painstaking and apparent, when one recalled the opposite conditions so glaring in other institutions elsewhere on the continent. The result of all this care is a homogeneous whole, simple and complete with results in keeping. Here the much vaunted box is unnecessary, the individual isolation of one little patient from the other is accomplished through intelligent cooperation of an exceedingly intelligent and conscientious nursing personnel. I need not say in view of all that has been said that each infant has a thermometer and other necessary utensils for its own use. Thus an infant who enters this institution does not become ill if well, and if ill there is no other infection contracted in the institution.

In this institution, we can at once understand the *raison d'être* of a special care of the infant. The other institutions, both new and old which I have seen, do not impress one in this way. They are simply collections of infants, nothing more. Infants are born in the house in the Keller institution, as well as brought into the house from the outside. The mothers are cared for before confinement in a separate service in another part of the house and do not obtrude themselves into the general institution. Here also both in the care of the future mother, in her confinement, the most exquisite cleanliness is observed, but above all simplicity; none of the gaudy, showy confinement rooms seen everywhere, especially in institutions bent on being quite up to date.

CHILD WELFARE DEPARTMENT

An institution devoted to the care of infants can never be complete without looking to their care when discharged from the institution, and this is done in a separate department which, by the by, is not the case in other institutions devoted to the care of infants exclusively. That is, there is a department of *Säuglings Fürsorge* — "child welfare." This is a separate department. We have something similar to it in New York in

the welfare department connected with some of our institutions, but only in a fitful, non-methodical way, scarcely deserving comparison with what is seen in Keller's institution and in others in Germany.

To return to the subject of infections and the *raison d'être* of the institution for the care of infants exclusively, from what has been said, even the casual observer cannot but be impressed that the best results can only be accomplished in this way. On the other hand, it must not and cannot be maintained that as to the scientific care of the infant that it is, as some would have us accept, something mysterious or requiring on the part of the physician a special training outside of the lines we have indicated; in other words, the care of the infant as seen in these institutions is not a full specialty of pediatrics. This would be an absurd contention to my mind, and not at all granted by anyone with whom I have spoken. The institution devoted to the care of the infant simply carries out detail to perfection long known to us but impossible in institutions where services are of a mixed character.

THE BOX SYSTEM

The box system of construction in wards of hospitals reaches its highest development in the hospitals of Paris and France. The origin of the box is a matter of interest and must have been due to an effort to diminish the chances of infection of one patient by the other. Of course the box alone would not do this, but with the box there go certain precautions which in themselves would, if carried out, reduce the chances of infection, and thereby mortality. The hospitals of older construction and the old wards in Paris hospitals for the care of infants and children, even on a casual inspection demonstrate why a decided effort was made to reduce infection and thereby mortality. Without entering into an unnecessary analysis of the construction of the old hospitals, it is enough to say that with the appearance of the box the conditions have remarkably improved, but whether this is an argument in favor of the box system or the greater asepsis and isolation exercised, is another question.

We have in the French hospitals devoted to the care of infants and children several varieties of box construction. Beginning with the old hospitals such as that of the Hôpital des Enfants Malades, boxes are constructed in the old wards and in the newer pavilions, which are about 10 years old. In the old wards of Hutinel the box is a small room about 8 feet by 10, the partitions reaching to the ceiling; the construction is of glass and wood, and the box is entered by a door which is supposedly

closed all the time. There are four or six such boxes in a ward. The box really is a glass room with a window leading externally, with plenty of light and sun and ventilation only through the window. In these boxes there may be two or three children; they may have the same affection or different affections; they are of the non-contagious type. The patient is placed in this box room when admitted to the ward, so as to guard against infections of other patients in the ward, should a case recently admitted develop measles or scarlet fever. In other words, these boxes may be utilized and are utilized as a species of reception ward. Outside the boxes there are the regular ward patients, also non-contagious. The nurse as she enters the box is supposed to exercise certain precautions. Even though the patient may not suffer from any communicable affection, she has a gown to be put on when she is in the box; the gown hangs on a peg inside the box. The patients in the box have utensils such as thermometers and pans for their special use. In this way, certain definite precautions can be carried out as to cleanliness and asepsis. This is the most primitive form of box system in the old wards. In other words, the boxes may be found more numerous, but they all have about the same form and are seen at one end of a ward.

In the new pavilions devoted to the care of measles, scarlet fever and diphtheria, the more recent construction of box is seen. The construction in the pavilion devoted to measles is of steel and glass partitions which extend along the side of the ward; the partitions are situated as a rule between the windows; they do not reach to the ceilings and project out into the ward for a distance of 6 or 8 feet, leaving a central corridor running through the wards from one end to the other. Thus in this system the tops and the front of the box are open and the arrangement is that seen in an old English inn, where recesses divide up a central room. The partitions being lightly constructed of steel and heavy plate glass, there is no obstruction to the circulation of air or light. In each one of these recesses there is a bed. At both ends of the ward are rooms constructed in the shape of boxes, the partitions reaching to the ceiling and entered by means of a door, and in these glass rooms or boxes are placed complicated cases, such as measles and bronchopneumonia. In each box there is a gown for the nurse, a basin, a thermometer and other necessary utensils for the use of the inhabitant of the box. It should be remembered that the tops and front of these boxes are open; therefore, later on in discussing the mode of propagation of infections, it will be seen that in such a box the question of infection through the atmosphere

has not been entertained. All the cases are cases of measles. If there happen to be mixed cases such as diphtheria and measles or measles and bronchopneumonia, they are placed in closed boxes, possibly in the same ward, as indicated at either end of the ward. In the pavilion devoted to scarlet fever, much the same form of box exists. In the diphtheria pavilion, however, there is the closed form of box; that is, a ward along the sides contains ten or twelve roomy boxes, the partitions reaching to the ceiling constructed of steel and glass, air tight; there is a window in most of the boxes leading to the open; the ventilation is further provided for by flues in the ceiling. The box is closed with a glass door and in the center of the ward is a large corridor. Thus passing along the corridor, everything in the box is visible from almost any part of the whole ward. One or two or even three patients may be in a box if small infants; generally two are seen in a box. In the diphtheria pavilion, the closed box is adopted with a view to flooding the box if necessary with vapor of steam or chemicals. The history of the patient and his progress and the disease is posted outside the box, in the main corridor of the ward. Thus the physician may not enter the box unless called on to do so. In the box there is the coat for the nurse and the individual utensils of the patient.

In this form of box, which is the most perfect and expensive, a thought was evidently given to the possibility of air as well as contact infection. It is evident, however, that if the primary idea was the separation of one patient from the other, this has given way to the idea of separation of the patients in groups of two or three, so that if an epidemic of mixed infections did occur it could be most easily held in check in this system as well as the system of one patient only to a box. Tube cases are generally separated in box rooms at the end of the ward. I saw two and three tube cases in a box, so that even here the individual separation did not obtain, except that in this large box room there are found low glass partitions between the beds on one side of the room and not on the other.

SERVICES OF BARBIER AND LASSAGE

The Herold Hospital in Paris is devoted entirely to the treatment of sick infants and children. In this hospital the box system is general and the wards are constructed on this plan even in the pavilions devoted to the care of patients with general internal, not infectious, diseases. The boxes are of recent and older construction. In the same wards the boxes are open at the top and extend from the floor to about 8 feet above, and

are made of sash, wood and glass and provided with doors. In some services, such as that of Barbier, these doors may remain open; in others, such as that of Lassage, they must be closed and kept closed. The boxes are aligned along the sides of the ward and in the center there is a broad corridor. Walking through this corridor, everything in the box is evident. There may be one or two or even three patients in a box. The diseases are mixed and there may be a bronchitis and chorea in one box with an enteritis. Each box is provided with a gown for the nurse and the patient's utensils, including thermometer, are provided.

DIPHTHERIA

In the pavilion devoted to the treatment of diphtheria, the box is closed at the top, reaching to the ceiling, and is provided with a system of ventilation. In some wards such as that of Lassage, infectious and communicable diseases, such as scarlet fever, may be seen in one box, and next door chorea and bronchitis or tuberculosis, and these particular boxes I have seen are open at the top and there is free circulation of air from the box into the ward. I understand that Lassage rarely touches a patient and only goes into the box in general rounds, if some special occasion arises, not otherwise. Another noteworthy arrangement is that very young infants are found side by side in the same box with older children; there is no arrangement as to age. Each ward houses upwards of thirty patients, and there are nearly 250 in the hospital. In this hospital the tuberculous cases are housed in pavilions apart from others and are also put in boxes. They are treated also during the day in the open.

PASTEUR HOSPITAL

The highest development and application of the box system is seen in the Pasteur Hospital. This is of recent construction and the whole hospital is on the box plan and is in direct touch with the Pasteur Institute with its laboratories. There are several pavilions each two stories in height. Inside, the ward is divided into a series of large glass and steel rooms; the walls of these rooms extend to the ceiling; they are of light steel and plate glass construction. Each box or room is closed air tight by a door and the ventilation of the room is accomplished by means of air shafts in the ceiling and windows leading to the open. The sun and air reach all portions of the pavilion. All the boxes open into a broad corridor and from this corridor everything in the boxes is visible to the observer. Passing along the corridor one can at a glance take in

the situation in any given box. Here is seen a complete mixed service. The exanthemata and infectious diseases are seen in one box and in another the diseases of a non-communicable nature. The doors of the boxes are kept strictly closed. The patients are of all ages, and, as remarked, there is a general mixed service. Of course we do not find in the box of a scarlet fever patient anything but that disease; the same with diphtheria. Here I also saw in boxes three cases of sleeping sickness, one in a child who occupied a box with another child who had another affection. What impresses one in the Pasteur Hospital is that in the development of the box system there has been a sacrifice to an orderly arrangement of diseases and patients.

HEUBNER — THE CHARITÉ

Returning to Germany, we find the box system adopted in the newly constructed hospital of Heubner, the Charité. Here the open partition of steel and glass has been adopted in one of the wards and this is called the box ward. The partitions extend up to the height of about 6 feet from the ground, are constructed of steel and glass, and open without doors into the center of the ward which is free and clear. Each boxed partitioned space contains a bed and the most diverse non-contagious diseases are housed here — tuberculosis, enteritis, chorea. Each so-called box extends out into the ward about 6 feet. There is thus free circulation of air and plenty of sunlight. Some of the little patients if able to be up may come out of the box and play in the corridor at the opening of the box. Each box is provided with a gown which the nurse is supposed to don when she enters the box. Each child is provided with separate utensils. The ages are mixed. There are other wards in this new hospital devoted to young infants, and these, as well as the wards which contain older children, are constructed without boxes. I understand a new box ward is being constructed to house the exanthemata.

DISCUSSION

The box system may be looked at from several angles and the impression on the whole is not satisfactory until one has visited a new institution like that of Keller, in which no boxes exist and in which infections are exceedingly rare. Thus the first definite point to be fixed in my mind from the start was that, given good, conscientious nursing and care in detail, the box system is unnecessary in a non-contagious service to the extent which I shall point out. The primary object of the box has been

to avoid infection. Some clinicians, as Barbier, wish to avoid principally contact infection, and others, such as Lasage, lay considerable stress on the atmosphere about the patient as a carrier as well as in contact infection. As a matter of fact, after a close study of the box system, we can conclude that it is a potent barrier to contact infection, and also to infection in the immediate vicinity of the patient; that is, in a tracheal diphtheria the expectorated masses never reach the next box and patient and this alone is a vast gain, preventing, as it does, not only mixed infection, but the reinfection of patients. On the other hand, in a ward such as the Lassage ward, in which contagious and non-contagious diseases are treated, and in which the boxes are open at the top, we would look for a very potent argument against the so-called atmospheric mode of infection. I understand that an infection of a patient with scarlet is rare, though they may be in the next box and at the same time this fact is a strong endorsement of the nursing in this particular ward where patients are handled very rarely except by the nurses, and in which the lack of contact infection is distinctly evident.

Therefore, if the infectious diseases can be practically treated in the same ward in the manner indicated, we certainly in the past have overestimated the importance of the agency of the atmosphere in carrying infection. Has the box system diminished the chances of infection? It certainly has in France by inculcating the importance of attention to detail, but behind this we feel that in wards in which non-contagious diseases are treated, the box is an unnecessary institution, if the nursing and attention to individual isolation of the patient as practiced in the wards of the Keller institution and the Mount Sinai children's wards are carried out. In medical wards only do I see the superfluity of the box.

In surgical children's wards, I should think the box would be a boon in emphasizing the isolation of one child from the other on account of the possibility of infectious matter of one patient reaching the neighboring bed, or the possibility of treating with the aid of the box, erysipelatous and infectious gangrenous conditions in the wards. In surgical wards it is my experience that the exanthemata are apt to break in on the surface, because assistants and nurses are not alert enough in detail of individual isolation of patients as in medical services. In such wards, simple partitions such as are seen in Heubner's box ward would serve all purposes of isolation, and would not interfere with light and air. I think a close study of the box system would in purely medical non-contagious services cause its rejection as a universal necessity. It may

be of use in the sense that Hutinel employs it in the ward as a temporary reception ward, either for doubtful cases or those children who as yet have not had the exanthemata. In the treatment of the exanthemata, diphtheria and measles, as also small-pox, the box not only is a means of cleanliness, but of prevention of reinfection and mixed infections as noted above. One can only reach this conclusion by a survey of new institutions, as those in New York, in which diphtheria and the exanthemata are treated in general wards, and those in Paris, in which the children are separated in groups in boxes. The latter system is certainly more cleanly and leads to better results.

THE ACUTE INFECTIOUS DISEASES

A study of the box system in an institution, such as the Hospital Pasteur, and then a close analysis of the results as published in the recent report of Dr. Martin, lead to the inevitable conclusion that in this hospital they certainly have solved one of the most important questions in connection with the treatment of these diseases, namely, the prevention of the mixed infections. Especially interesting are the results obtained in the management of cases of scarlet fever, measles, diphtheria and varicella. The mortality in these diseases for a period of ten years, allowing for varying severity of epidemics, is not only low, but remarkably lower than that of any other similar number of cases in other hospitals, and more especially is this low mortality rate noticeable in infants and children below the age of 2 years. When compared to the mortality rate in hospitals in which the children are treated in the old way in hospital wards, the conclusion is that in the Hospital Pasteur, even if some of the old ideas, and new ones for that matter, as to the arrangement of patients as to age are roughly set aside, the results are convincingly in support of the contention that the system of individual isolation is the only and correct one to follow in the future management of these diseases. I speak only of the exanthemata; not diphtheria. In the Hospital Pasteur mixed infection and reinfection is reduced to a minimum and is rare. Not only is this so, but there is a feeling that the crowding together of forty or fifty cases of scarlet and measles in one open ward not only is a potent factor in causing incontrollable mixed infection, but is one of the chief sources from whence flow an increased mortality. In the old system, as is seen even in the new hospital for contagious diseases in New York, even if the nursing is beyond criticism, it is hard to see how one can avoid carrying infections from one child to another. Especially when beds

are close to one another, with children coughing and expectorating, nurses passing from one to another, sometimes washing the hands, at others not doing so. Hence the mortality-rate cannot begin to compare to what is seen in the Hospital Pasteur.

I have described the system of box isolation constructed here, but have not mentioned that daily there is a complete sterilization of eating and other utensils used by patients, so that every day brings practically a sterile set of apparatus to the patient's bedside. Vigilance is ever present to carry out details of nursing and treatment and at the same time there is not such a superfluity of nurses as to be noticeable. It should be kept in mind that all the exanthemata are treated in the ward where contagious maladies are housed, and though not in the same box, a scarlet may be in one box and measles in the next and still no transmission occurs to any appreciable degree. In ten years the number of infections in the hospital proper were thirty in an aggregation of 9,677 patients. Most of these infections in the house could be accounted for by an infringement of the rules laid down for the management of the patients and boxes.

An amusing example is as follows: In order to entertain some children convalescents from scarlet and measles, a phonograph was placed in the corridor; the children could not very well hear the music, so that the sisters opened the doors of the boxes, to allow the children to see and hear. When the backs of the nurses were turned the little ones escaped into the corridor, mingled with each other, and in fourteen days they contracted measles. "Now the doors of the boxes are kept locked when the phonograph plays."

STATISTICS

Some of the methods are of note. All infants and children on entering receive an immunizing dose of diphtheria antitoxin no matter what their malady. Taking scarlet fever the mortality below 2 years of age in seventy-one cases is 8.4 per cent.; from 2 to 14 years in 798 cases, 0.9 per cent. Certainly this is astonishing. Measles, 245 cases below 2 years of age, give a mortality of only 9.8 per cent.; 260 cases, from 2 to 14 years, a mortality of 1.10 per cent.; diphtheria, 309 cases from 0 to 2 years, give a mortality of 20 per cent.; 437 cases from 2 to 14 years of age, give a mortality of only 6 per cent. I know of no such favorable statistics or anything like them elsewhere. Dr. Martin has compared his statistics with similar statistics of an equal number of cases in other hospitals where patients are treated in open wards and without

saying much as to such comparisons and allowing for all sources of difference, the comparison leads to only one conclusion, and that is that there is only one method of treating the infectious exanthemata, and that is in the box system. The old system of general wards even with isolation rooms is a system of the past. Not only is this true in considering the mortality rates, but what is vastly more of scientific interest and importance, the avoidance of the mixed infections. Even in hospitals and wards where non-contagious diseases are treated, if there should arrive a case of measles or scarlet fever, its isolation in an outside box is preferable for many reasons to its transfer to an isolation ward where the case passes from the control of the attending physician to the hands of another and the patient suffers.

It would seem that the maintenance of separate isolation wards is an extra drag on the service, and though it is a spiritual comfort to banish a case of measles to where not a soul can get at it except those in the isolation ward, the Pasteur system proves to my mind that this is a needless procedure. Moreover, it must not be forgotten that in the Pasteur system special nurses do not come for the exanthemata, but the same nurse after the precaution of changing her gown in the box and washing her hands, passes from a child with one contagious disease to another with a different contagious disease. In the face of this some of my experience in the past and some of the criticisms to which my views have been subjected seem certainly amusing.

ISOLATION BOXES IN NON-CONTAGIOUS WARDS

In constructing children's wards to-day, it would be wise to have in connection with such a service where general non-contagious diseases are treated, several boxes for the immediate isolation of cases of measles or scarlet fever which might break out in the service. They could be so constructed as not to interfere with the general ward, but be placed outside of it. In this way, the early isolation would tend to prevent epidemics and also the cases would remain under the same attending service and observation. In a way this has been done both in the medical and surgical services of the Mount Sinai Hospital without any appreciable ill effects. Cases of varicella, diphtheria and scarlet fever have been placed in rooms outside the general wards where some special reason made it unwise to lose sight of the patient. But here a special nurse was placed in charge. Whether in the future we shall in other institutions follow this system or that of the Pasteur Hospital will be a matter of scientific interest.

A study of the Pasteur system also is a convincing argument against the potency of atmospheric infection. What amusing and annoying blunders and injustice have been committed in the name of the atmospheric theory, the life work of every sincere clinician will show. There was a time not long over a decade ago when wiseacres shook their heads when the primary importance of contact infection was a matter of discussion. Even to-day, and in Paris not far from the Pasteur, there are those who will not entirely allow the absurdity of some of the old propositions as to the agency of atmospheric contagion. In New York we can see that the times are still with the atmospheric as well as the contact theory, and while admitting the importance of contact infection, the mysterious fetish of atmospheric agencies certainly holds in fetter some of those whose influence counts for something.

DISCUSSION

DR. NORTHRUP: I should like to ask Dr. Holt and Dr. Koplik how much they believe in the danger of the presence of the Klebs-Loeffler bacillus in the nose of patients not having diphtheria and of vaginitis with the presence of the gonococcus by smear without any discharge? Perhaps we have been a little hysterical over these matters. It seems to me the presence of the bacilli without lesion is not very dangerous, nor, perhaps, is the presence of the gonococci, without discharge.

If any one is especially interested in the subject of guarding hospital wards against contagious diseases, and in contact infection, he will find a great deal of satisfaction in reading Dr. Doty's recently published book in which the whole subject is thoroughly portrayed.

DR. HOLT: I can add one case of recurrence of scarlet fever. It occurred in a relative of mine, the first attack being at the age of 7 or 8, and the second at the age of 24 years; the last attack being the past winter. Both were severe and typical. In the first there was an otitis and in the second a nephritis.

Regarding the treatment of children whose noses or throats show by culture the presence of the Klebs-Loeffler bacilli, without symptoms or visible lesions, my own practice has been not to remove them from the ward. To secure a certain amount of separation, we have had constructed in our wards two or three alcoves, each having a single bed. There is a marble slab set in the wall about 4½ feet in height and projecting about 2 feet beyond the length of the bed. Such separation seems to have been of some advantage. We have had a large number of children in the wards in the last few years that have shown the Klebs-Loeffler bacillus in the nose or throat, but very few cases of real diphtheria. We fear the cases showing bacilli by cultures, but no other symptoms, much less than formerly. They are carefully watched, however.

As to the danger of infection from cases in which the vaginal smears show the gonococci, but no discharge is present, I am not yet prepared to speak positively. Such cases should be watched closely and, I believe, not placed in the same ward with other female children. I have given up for all these patients the use of napkins and have used in their place a small mass of absorbent cotton with a square of cheap unbleached muslin. This can be burned when used. That change has done much to reduce the frequency of these infections in the wards.

We follow the practice of taking smears from all cases on admission and of taking smears of all girl patients at least once a week. By these means, together with others, such as separate thermometers, etc., we have had no general spreading of vaginitis in the wards for several years.

The worst hospital infections, as far as my experience goes, are those of the respiratory tract, and how to prevent these is, I think, our great problem. We have been helped in these cases by making cultures from the bronchial secretions to determine the nature of the infection. Cases with a good deal of cough and secretion we separate from others in the ward by the alcoves.

DR. KERLEY: I wish to report two cases of recurrence of scarlet fever, one a girl 12 years of age, who this year had a second attack, after an interval of four years. She is the daughter of a physician and was seen on both occasions by an inspector of the Health Department and myself. The other was a boy whom I saw in his second attack which occurred five months after the first, and both the family physician and the mother stated that the child had desquamated freely after the first attack. The second attack was unquestionably a true one. The child died on the fifth day of the illness.

DR. JACOBI: A friend and practitioner of New York told me a number of years ago that he had seen a case in which the child had had scarlet fever eleven times. I asked him to let me see the next attack, which he did. There was fever, eruption, red tongue and sore throat. It was easy, however, to convince ourselves that it was a case of intestinal autointoxication. If a good purge is given in the beginning, these conditions do not last long. In a long life I have seen but two cases of recurrent scarlet fever, but they were decided cases, and I saw both attacks. There was fever, eruption, desquamation and, in one, nephritis.

So far as vaginitis is concerned, I am still of the opinion that there is nothing more dangerous than that. It can be treated easily, but cured with difficulty, and sometimes treated with no result at all. There will be relapses all the time, every two or three months a return of the trouble. The explanation is easy. The gonococci disappear from the little vagina, but remain in the uterus. The uterus of little babies is not the same as that of older children. Up to the seventh or eighth year it has a surface that is not smooth. There are furrows and wrinkles, and in these the gonococci remain. They may not show their presence for two or three months or more at a time. Then when there is some secretion they reappear and you have the same condition of affairs all over again. I have seen cases lasting for years, relapsing from time to time, seemingly absolutely incurable. I am sure many of you have seen these cases. That is why I fear vaginitis more than anything else, and the precaution of examining these children at least once a week is a very important one.

As far as the presence of the diphtheria bacilli in the nose is concerned, we should be very careful in discriminating between whether the Klebs-Loeffler bacilli are found on intact mucous membrane or mucous membrane that is not intact, and that is difficult. Most of us have some bacilli on the mucous membrane, different germs in our throats and in our noses. It is of no importance so long as the mucous membrane is intact, but as soon as the mucous membrane is not intact the microbes slip in. It is just so with diphtheria of the nose. During an epidemic almost everyone has the bacilli in the nose, and if we could examine every school child at such times we would undoubtedly find them. It is not dangerous unless there is a catarrh that allows the bacilli to penetrate. On the other hand, there is, of course, no more dangerous thing than nasal diphtheria. The bacilli on mucous membrane that is ulcerated are very dangerous. The causes are often mixed infections. Forty years ago almost every child with a

mixed infection died. Rodger said that every case of nasal diphtheria was fatal. We in America have modified that by keeping the nose washed out. I have no advice to give in connection with the question of the presence of diphtheria bacilli in the nose and throat of the school child. Is it really necessary to isolate such children; to keep them imprisoned, as we have isolated and imprisoned against all rules the typhoid carriers? I do not know.

DR. ROTCH: While I believe that the presence of diphtheria bacilli in the nose is not dangerous to the individual so long as there is no lesion of the nasal mucous membrane, yet it is possible that these cases may be carriers and convey the disease to others. It is also difficult to eliminate the possibility of lesions in the mucous membrane of the nose and throat. A large number of children are likely to have such lesions. We have had cases in which in isolating children, with no lesion in the nasal mucous membrane of the child, the nurse isolated with the patient, has contracted diphtheria. Antitoxin is of no advantage in these cases because, though the bacilli are present, there is no infection.

DR. MACHELL: I had a case of recurrent scarlet fever in which there was definite sore throat, rash, otitis and desquamation. The patient's father, who was a physician, said that she had had a previous attack of scarlet fever undoubtedly.

DR. MORSE: Our experience with these cases of diphtheria bacilli in the nose has been that they are dangerous to those about them. At the Infants' Hospital we have for many years been immunizing with antitoxin all the babies that come into the hospital. We have not had a case of diphtheria develop in the babies in the hospital, but have had it develop in the nurses and scrubwomen. When this has happened we have almost always found babies with a slight nasal discharge and the Klebs-Loeffler bacilli in the nose.

As to the box system, it seems to me, without any practical experience, that it must be bad for the patient in the boxes. How can they get proper ventilation and be prevented from reinforcing themselves?

As to the prevention of infections in general in hospital wards. We are just beginning to build a new Children's Hospital in Boston and have adopted the plan of building pavilion wards two stories high, each story to have two wards of ten beds each, and two isolation rooms. If there is a suspicious case it can be put in one of those rooms. If a contagious disease develops, we thus have only a ward of ten beds infected. We are also going to have two unoccupied wards, so that if a contagious disease develops in a ward we can stop admission to that ward, open another, and when the first is out of quarantine reopen it. We have thought this would be the most feasible plan and better than having isolation wards.

DR. EATON: As to the recurrence of scarlet fever, my own family history says that I had it twice. I can remember the second attack. Some one has remarked as to the infrequency of repeated attacks of measles. Last week I discharged from observation a little girl whom I know has had true measles twice and German measles once. In the attacks of true measles she was under my observation from the beginning.

DR. CHURCHILL: One aspect of this question of gonococcal vaginitis not spoken of is its latency. We have all seen where, without rhyme or reason, without having had a case for months, one suddenly develops out of a clear sky. At the Childrens' Memorial in Chicago we have taken to sending our social settlement

workers into the homes of these children and they have found in a number of instances that there has been gonorrhea in other members of the family, and now one of the questions we ask when these children come for admission is as to the presence of any venereal disease in the family. Of course, we cannot always get at it in that way, but a good many admit it. These children may come in with a latent condition which will flare up later. Many of these infections are contracted in the homes really and not in the hospital. We should, however, take every precaution in the hospitals to guard against such infection. Personally, I dread it more than any other infection that we have, and I should like to see this society take up an exhaustive study of the question, an investigation of this matter in the hospitals to see what method of treatment may be most practical for its avoidance.

Dr. Morse has spoken of their new hospital in Boston; we are also about to add another pavilion to our hospital and are building it in this way: there will be a main building of two stories, and on each floor there are to be six small wards. Then running out from the main building will be three separate pavilions to which we shall transfer our cases of contagious disease as they arise. The object of making so many small wards is to put the different cases as they come in into wards any one of which can be isolated if an infectious disease develops.

To return once more to the question of vaginitis, we take smears of every girl patient that comes in and then take them twice a week during the stay in the hospital. I think this precaution should be taken.

DR. CAILLÉ: During the last twenty-five years it has been one of my duties to try to keep contagion out of the children's wards, and I suppose I have succeeded as well as the next man. It is too late to go into details, but my conviction is the same as that of Dr. Koplik, that it is mainly contact infection that we have to deal with. If this is correct Dr. Northrup's grille is valuable to a certain extent. Some twenty years ago, in talking with old Dr. Bouchut of Paris at the Berlin International Congress about keeping diphtheria and other diseases out of the wards, he said: "I am not afraid of diphtheria—I place a high screen around the beds; diphtheria cannot jump more than six feet." That was in 1890.

Another thing—if you wish to keep the wards clean, keep the surgeons out with their nose, throat and ear cases. The moment such cases are admitted, particularly those showing a purulent discharge, there will be trouble.

DR. PISEK: As to the quarantine of cases showing the presence of diphtheria bacilli in the nose, if we could get the bacteriologist to determine by more ready methods than we have at present, the virulence of the bacilli, we could decide which cases to regard as dangerous to other children. Work is being done along these lines at present, and it is probable that before long we will have some such method of differentiation.

DR. BLACKADER: I confess that I would not like to depend on these boxes, or screens. As a resident in the London Hospital it was very common for us to put a screen around the beds and during my tenure of office there was not an instance in which the disease spread. I scarcely think this a modern idea. Some time we may be able to examine these cases more thoroughly and differentiate them better, but until then I should like something more than a mere partition.

DR. NORTHRUP: There seems to be a little confusion of terms. It is not an incomplete partition, but a screen. In the Paris hospitals they have this grille and also the box. The box is 8 feet high so that the nurse goes into a sawed-off room, as it were. But this grille they put around the bed. I am only copying their

grille and that is what I have referred to. There is no difference of opinion about the matter of the Klebs-Loeffler bacilli in the nose, but we take individual precautions with all these cases. Every patient that is in bed is quarantined, although only 4 feet from his neighbor.

DR. SOUTHWORTH: Thus far to a large extent the discussion has centered around hospitals. The question applies very strongly to institutions as distinguished from hospitals; that is, institutions in which the hospital feature is secondary. It is of the greatest importance in institutions where children are presumably well that they should be protected from infection. The old ward plan of the institution has been that of caring for the largest number of patients with the smallest number of attendants, and that means, of course, the large ward with many beds. I understand from Dr. Morse that in Boston they are about to build their wards with only room for ten beds each. That is decidedly a step in the right direction. If anything I should think it advisable to make them even smaller. I thoroughly agree with Dr. Holt as to the danger of different types of infection. Certainly in my own experience the mortality has not been as high from the ordinary exanthemata as it has been from the respiratory infections—the influenza types that Dr. Holt speaks of. For the last three winters our chief infections have been of that type, and the direct and indirect effects have shown themselves particularly among the bottle-fed infants. The only way that such infections in institutions can be remedied, if not by this plan of alcoves or grilles, is to reduce the size of the wards so that the opportunity for infection shall be less. Our President recently wrote an article, and a very able one, in which he expressed the opinion that the knell of institution life for infants had been sounded. A few of our institutions are certainly reaching the limit of what we can do, and if we are to still further reduce the mortality we must do it by limiting ward infections, particularly of those diseases to which too little attention has been given, namely, those of the respiratory tract.

DR. ADAMS: I believe I am responsible for the discussion of the subject of the recurrence of scarlet fever, and I am more than satisfied with having propounded the question at the last meeting of the Society, since a man of such wide experience that he is now attending the grandchildren of patients he had in their infancy, has only seen two cases of recurrence of scarlet fever. It has been so often my experience that when the supposedly second attack had run its course the parents have said, "Well, if this is scarlet fever, then my child never had it before," that I wanted to know how many of the members had themselves attended a *bona fide* case of secondary attack of scarlet fever, and we see how few they are.

As to the ward problems, it is as though we were at the Ulster county fair the way we have been talking about box stalls. The question arises, how much air space are the infants going to have in this way? I take the ground that it is not well to pen up a patient in this way without plenty of air. I believe we have recently constructed in Washington as large a ward for children with as few beds and as great air space as any in this country. It is a large room with plenty of windows. In that hospital we have recently had an epidemic of measles and we have tried the pen plan, not as complete as that of Dr. Koplik, but more so than that of Dr. Northrup. The question now arises, how to keep the children who are running around in the wards within bounds. Babies, of course, you can treat in this way, but it is impossible to keep the older children from running around to the other beds.

DR. NORTHRUP: That is where these screens come in.

DR. ADAMS: But they will go behind them.

Another factor is that in some of the hospitals there is such strong sentiment against it. If you have the same sort of ladies to deal with that we have, and let a contagious disease stay in the same room with the other children, some one will be looking for another job. We recently had that experience with poliomyelitis. The board rounded up the staff and thought it had not done its duty in this respect, though it was shown that it had.

DR. LA FÉTRA: The subject of the recurrence of scarlet fever was the one I assumed to be before the society, but since measles has also been referred to, I would say that I have seen two cases of recurrence of measles; one a child of 8, who had had an attack previously at the age of 6. The other instance of recurrence of measles occurred in a family of 3 children. I saw both the attacks; all the three children were affected each time, the interval being two years.

DR. FREEMAN: There is a modification of the box system that has not been referred to which is in use in the large children's hospital in Paris. They have separate wards for contagious diseases, but in each general ward two beds have glass enclosures and in these beds are put suspicious cases, to remain until a definite diagnosis has been made.

DR. KOPLIK: As to ventilation, we must not forget that this is the *Hôpital Pasteur*, one of the greatest in the world, and the ventilation is, of course, perfect. These cells communicate with the outside world, through windows, and there is also a fan system of ventilation. Some of the cells are closed for the use of steam inhalations.

The statistics referred to were published by the Pasteur Institute and scientific men would, I am sure, not question them.

As to the recurrence of scarlet fever, I have been unfortunate enough not to have seen a case, but I have seen an instance lately in which I pronounced the disease scarlet fever in a child who had had the disease before. I questioned the mother very carefully as to whether or not she had given the child any drug, which she at first denied, but later admitted that a day or two before the patient had taken 10 grains of quinin. So there may have been a blunder.

As to the question of Klebs-Loefler bacilli; if by accident we find diphtheria bacilli in the nose and throat without local symptoms we put the patient in an outside room, put a gown there and gloves and cap for the nurse so that when she goes to the case she dons the uniform and when she leaves it she takes the proper precautions. We do the same with other infectious diseases, if there is any reason why the patient should not be sent away from the hospital. Some patients are too weak to be sent away. We never refuse a case of a very sick child with a vaginitis if we can help it. Lately I was called to see such a child and was not told by the parent, but learned later, that one of the hospitals in New York had refused her admission. I was glad to take the child in although the doctor told me that the patient had gonorrheal vaginitis. I put the child in the general ward, labelled the bed and took the proper precautions and have not seen any bad consequences. I have not noticed that it spreads if handled in this way.

We examine these little ones when they come in, taking smears, but if there is no discharge the staff are requested not to do this. It disturbs the child unnecessarily. If there is any discharge or redness the examination is made.

DR. CHURCHILL: What is the objection to taking a smear?

DR. NORTHRUP: As to the matter of scarlet fever, personally I should not hesiones, as you would want your own child to be treated.

DR. KOPLIK: I simply believe in treating the children, especially these little tate to treat scarlet fever in the ward with our grille. As to desquamating cases, I tell the staff that I do not care so long as the nose and throat are all right, and there is no ear discharge. These old traditions about scarlet fever being sent by a letter from the child to its parents I do not believe in. We must keep an eye on the germ and go after it, and the germ is in the moist mucous membranes.

THE TREATMENT OF SEPSIS IN SCARLATINA WITH ANTISTREPTOCOCCUS SERUM

MATTHIAS NICOLL, M.D.
NEW YORK

In using the term sepsis in scarlet fever I desire to be understood as referring to a set of clinical symptoms occurring forty-eight hours or longer after the onset of the disease, which are apparently due to the invasion of the body by organisms of the streptococcus group, which. up to the present time, are not known to possess any cultural or other characteristics which serve to distinguish them from streptococci isolated from a number of other morbid conditions. The symptoms may be briefly stated as follows: No fall of temperature, or a renewed rise; abnormal swelling of the mucous membrane of the throat, with or without superficial sloughing; profuse nasal discharge; marked cervical adenitis; rapid, often irregular pulse; mental apathy; active or low delirium. Streptococci may or may not be found in the blood, and it should be said that while they are usually present in prolonged cases especially, they are not necessarily so, even in those which must be clinically regarded as septic and, on the other hand, may be found at an early stage in cases whose course is otherwise benign and which do not admit of other than a technical diagnosis of this conditions.

Until the organism which causes scarlet fever has been definitely determined we must continue to regard those cases which are overwhelmed by the onset of the disease and are likely to succumb in twenty-four to forty-eight hours as directly due to this undetermined cause. Such are, in this country at least, of comparatively infrequent occurrence. The greater number of severe and fatal cases being of the class the symptoms of which I have described.

Scientific workers on the problem of scarlet fever seem more and more inclined to disregard the possibility, formerly so generally advocated, of streptococci representing anything more than the invasion of a secondary organism on a soil suitably prepared by some unknown agent. If this view proves to be correct, it must be confessed that certain well-authenticated phenomena are thus rendered most difficult of explanation. Of these I may mention the undoubted success of vaccination with killed

streptococci from scarlet fever patients as a means of preventing the latter. This work has been largely confined to Russia and apparently has caused but little interest in this country. Of the recent reports I may mention that of Tesjakoff, who in a study of 15,000 vaccinated patients, reaches the conclusion that three inoculations extending over two weeks is able to protect against the disease. Again Raíkowa, making observations in seven epidemics, on 721 vaccinated patients, found that among 524 patients vaccinated but once nine cases of scarlet fever occurred; among 22, vaccinated twice, five cases, while seventy-five patients vaccinated three times remained free from the disease.

Verhoff points out that the death-rate in 403 vaccinated patients in whom scarlet fever occurred was but 6 per cent., compared with a rate of 17.5 per cent. in the unvaccinated. Furthermore, all those who have made use of vaccination, from Gabritchewsky, who originated it, to the present, agree as to the common occurrence in those inoculated, of symptoms which cannot be distinguished from those of scarlet fever of the milder type as regards the onset, course, rash and occasional complications. Again, if the streptococcus be eliminated, how are we to account for the good results of the antiserum in Moser's fourth category of cases — those patients overwhelmed by the first rush of the disease — which showed a mortality of 100 per cent. without serum, and 65 per cent. or less with its use?

Two recent attempts to do away with the streptococcus as a causative factor are of interest. Cantacuzène, of Bucharest, reported to the Société de Biologie in April, 1911, that he had inoculated nine of the lower monkeys with bronchial glands, pericardial exudate and blood, the latter two free from streptococcus, taken from scarlet fever patients, and produced what appeared to be in all respects true scarlet fever, having an incubation period of seven to thirty-five days, and followed by typical desquamation. I am authorized by Dr. William H. Park to state that six monkeys (*Macacus rhesus*) injected with the blood of six different scarlet fever patients not tested for streptococcus, failed to show any symptoms of the disease, one dying after a few days of ileocolitis. Dr. George Bernhardt of Berlin, working under Gaffky, reported in April that by inoculating a number of lower monkeys with suspensions of tongue-scrapings, serum and enlarged nodes of scarlet fever patients, subsequently excising the enlarged inguinal nodes near the site of injection, grinding and passing the latter through other monkeys, he was finally able to procure nodes showing no streptococcus or other organism,

whose further inoculation into another series of monkeys caused symptoms in all respects similar to those in scarlet fever of human beings.

If this work can be confirmed, it must be conceded that the streptococcus can no longer be regarded as the causative factor or essential to its development. Until this is accomplished it would seem wise to have an open mind on the subject, especially as it is becoming daily more evident that with greater refinement of technic and newer methods of differentiation, we may soon be able to assign to the various strains of these organisms specific characteristics in the production of different morbid conditions, one of which may be scarlet fever.

The serum treatment of scarlet fever, first brought into prominence by Moser, whose name is usually associated with a serum produced by the inoculation into horses of streptococci taken from many patients with scarlet fever, was, like most specific remedies, hailed at first with the greatest enthusiasm, and, like most specifics, the results obtained did not fulfil popular expectations. If one consults the now fairly voluminous literature on the subject, he is sorely puzzled to account for the contradictory opinions set forth as to the worth of the serum. This, in part, is to be explained, I believe, by difference in the methods of its employment, whether used early, or only late, in moribund cases; differences in the type of the disease, not only locally, but as between different countries; and finally, by judgment founded on too few cases. There is, furthermore, undoubted difference in the antitoxic strength of sera and not unnaturally a prejudice against the use of the huge doses which seem essential to the production of results.

I shall refer to but one set of observations, those of Fedinski of Moscow, published in 1910, who in a most elaborate analysis of 317 cases in which serum was used, compared with about 900 cases without it, comes, as it seems to me, to the very reasonable conclusion that the serum given in full doses before the fifth day greatly increases the chance of recovery, even in the apparently hopeless cases; that in a large majority the temperature falls by crisis within twenty-four hours, or, if by lysis, the course of the fever is shortened. The occurrence of complications is less frequent and their gravity diminished. The influence on the heart's action, central nervous system, the rash and on necrotic processes is marked. The dosage in the average severe case was 200 c.c. subcutaneously, except in the case of young children, when 100 to 150 c.c. were given, and this dose was repeated in from twenty-four to forty-eight hours if necessary. Chart 1 shows the deaths from scarlet fever in the city of

Moscow for a series of years. The solid line represents those patients who died outside the hospital, the dotted line those receiving hospital treatment. It will be noted that the average of the hospital deaths held well above those dying in the city, but that with the beginning of serum treatment in the hospitals, and especially in the second year of its use when others than the apparently hopeless patients were thus treated,

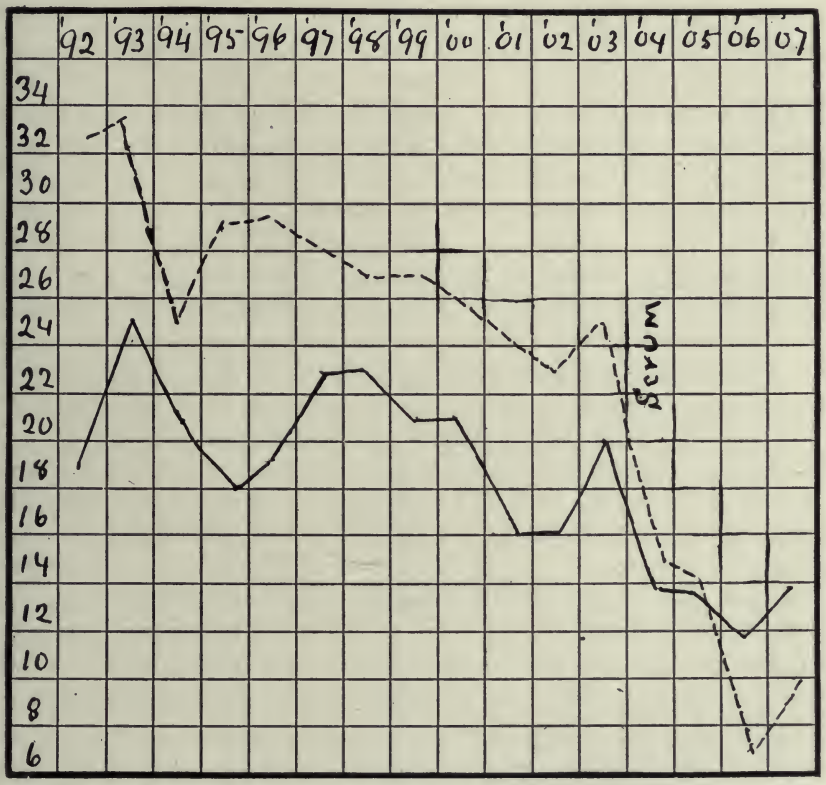


Chart 1.—The solid line shows the mortality curve from scarlet fever in Moscow from 1892 to 1897; the figures on the left show the percentage; the dotted line shows the mortality in the Vladimir-Kinderhospital during the same period under serum treatment.

the hospital patients show a death-rate well below those treated outside and without serum.

In this country the serum treatment of scarlet fever has, as far as I know, been but little tried. My own experience was obtained at the

Scarlet Fever Hospital of the Department of Health of New York City during February, March and April, 1910, in the course of a very extensive epidemic of the disease. The serum used was that prepared under the direction of Dr. Park, consisting of eleven strains of streptococci from scarlet fever patients—blood, throat, glands, etc., and one of streptococcus from a case of endocarditis. Owing to a somewhat limited supply at the time, it was thought advisable to give but 50 c.c. as an initial dose, which of course precludes the possibility of comparison with the European results. In so far as was possible in a badly overcrowded hospital, with overworked staff and nurses, every patient who showed markedly grave symptoms, regardless of the day of disease, was injected by the staff or myself and visited by me daily, with the exception of four cases furnished me by the resident physician. By no means all the fatal cases during these months were the patients injected, as measles, diphtheria and other complications accounted for their unfavorable progress and often death. Again, patients who, in spite of the severity of onset, seemed to be in no immediate danger, not infrequently took so sudden a turn for the worse that there was no opportunity to make use of the serum.

There were injected in all, thirty patients, of whom seventeen died; not a very brilliant showing, it must be confessed, but on analyzing the fatalities, the poor results may be reasonably accounted for without detracting from the value of the serum. Of these seventeen cases, four patients were brought in the hospital in a moribund condition, immediately injected, and died within a few hours. Of those who were ward patients twenty-four hours or longer, one died within two hours after receiving injection, two others within twelve hours, a length of time too short to hope for any relief from a subcutaneous injection. Another patient, after seeming to respond favorably, contracted measles and ileocolitis; another measles, followed by gangrenous varicella. The condition of three others was shown to be due to a complicating diphtheria which failed to yield to large doses of antitoxin following the serum. One patient was injected late in the disease, with the hope of affecting a double mastoiditis, 100 c.c. being given intravenously. The result was inconclusive, as an operation was thought desirable. Following this, the patient received 100 c.c. subcutaneously, grew gradually weaker, with no marked lowering of the temperature, which had been exceedingly high, and died two weeks dater in extreme emaciation. This leaves four patients in whom the failure of the serum must be accounted for on other grounds than those just described.

CASE 1.—H. H., aged 7, had been ill three days on admission; temperature 104.2 F., pulse 144, respiration 32; glands in the neck greatly swollen; patient looked extremely septic. The patient was given 100 c.c. of serum subcutaneously, pulse, respiration and temperature falling the next day and the temperature not going much above normal until just before death. Ten days after receiving treatment, the heart action became very unsatisfactory; the patient looked very pale and weak; stimulation seemed to have no effect, the pulse growing weaker and more irregular day by day. A few days later, the patient developed general choreic movements, followed by arthritis of the left wrist, and died three weeks after admission apparently of heart failure due to myocardial involvement.

I have the records of two cases similar to this in patients who were given 150 c.c. intravenously for a very grave mixed infection with diphtheria. The local throat symptoms cleared up readily under the combined use of antitoxin and serum, but the patients both died a week or more later, one with a very rapid heart action, and the other with a pulse which fell from 120 to 53.

CASE 2.—S. McB., aged 4, ill eight days; throat very much swollen; cervical nodes greatly enlarged; patient profoundly septic and delirious; temperature 104, pulse 180. The patient was given 50 c.c. of serum and died thirty-six hours later without any apparent amelioration of conditions. The failure of the serum in this case may be reasonably attributed to the length of time the patient was ill.

Following are two cases (3 and 4) in patients of Dr. Sexton, the resident physician, whom I did not see. They were, however, very carefully studied and the pulse and temperature taken every two hours, before and after the administration of serum.

CASE 3.—J. K., aged 2, had been ill four days on admission November 17, when the temperature was 103.4 F., pulse 140, respiration 32. This condition did not change markedly during the next five days. The cervical nodes were very much swollen; the pulse at times was imperceptible. On the ninth day of her illness, she was given 50 c.c. of serum and died thirty-six hours later without any appreciable effect having been produced.

CASE 4.—J. M., aged 16, was admitted November 14. November 23 the temperature was 104.5 F., pulse not countable, respirations much increased. The next day when the 50 c.c. of serum was given the temperature was 101.2 F., pulse 180, respiration 144. The patient was markedly septic, cyanosed, and wildly delirious, heart sounds muffled, pulse hardly perceptible. Temperature the next day was 100 F., pulse 160 and of a better quality; respiration 36. On the second day his temperature dropped to 97 F., pulse to 104 and respiration to 36. The patient was still cyanosed and very delirious. Mouth and nose discharged profuse bloody secretions. The third day the patient was still delirious, though the pulse was of better quality. On November 28, four days after giving the serum, the temperature was 100 F., pulse 152, respiration 36. The color was better and the pulse of a fair quality. Nourishment was taken well; nose and mouth were still bleeding. Later in the day, the condition became suddenly worse; the patient became cyanotic and died of heart failure.

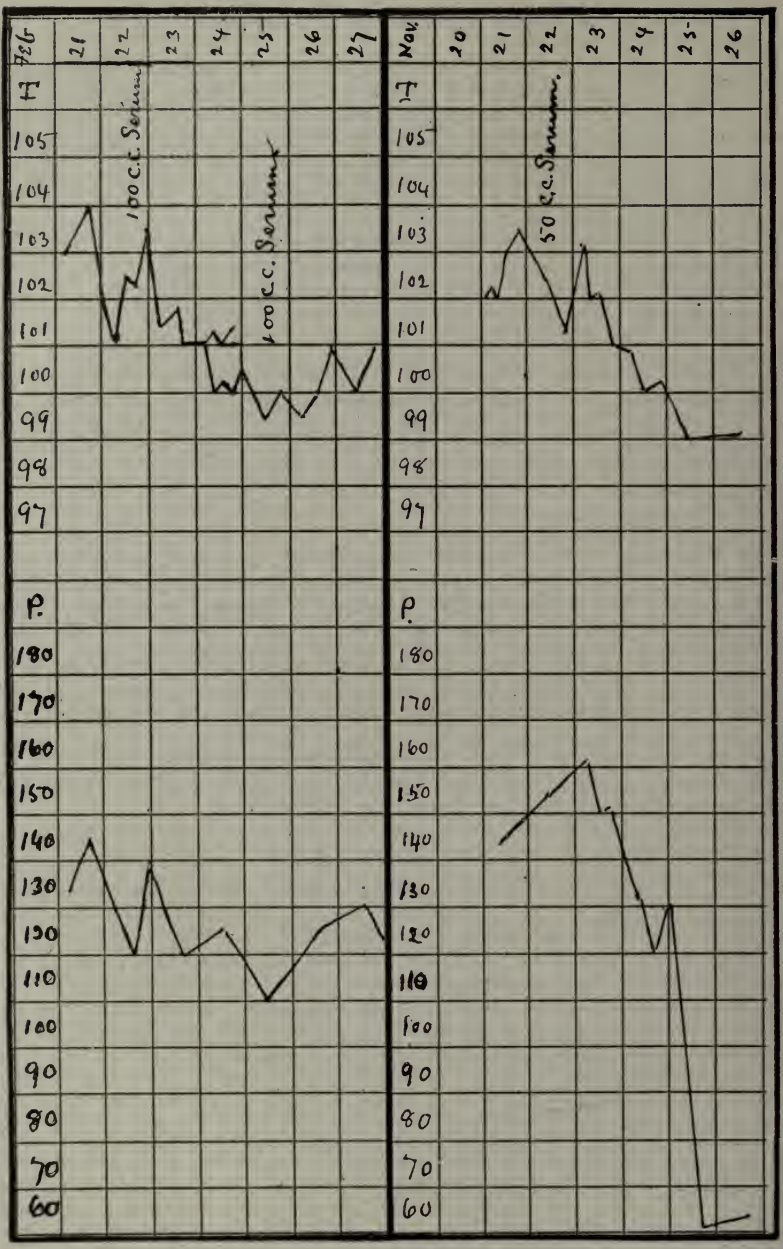


Chart 2. Chart 3.

Chart 2.—Shows the effect on temperature and pulse of serum administered in Case 5.

Chart 3.—Showing effect of serum treatment in Case 6.

If the serum had been given in anything like sufficient quantities at an earlier stages in these two cases, it is possible that it might have been successful in its action.

Of the patients who recovered, a short history of a few will serve to show the apparently good effect of the serum.

CASE 5.—S. K. (Chart 2), aged 10; ill two days on admission; covered with an intense dusky rash with much vesiculation; throat and cervical lymph-nodes very much swollen; lips dry and fissured; constant muttering delirium; 100 c.c. of serum given subcutaneously. The next day the temperature fell; the delirium continued. The following day, 100 c.c. serum was given. There was a general and profuse desquamation over the whole body; the patient was not delirious, but very stupid. The day following there was a marked improvement in the general condition. The subsequent history was one of convalescence, interrupted by multiple arthritis in the third week. The patient was discharged in good condition after a long stay in the hospital.

CASE 6.—E. R., aged 7 (Case of Dr. Sexton). The patient had been ill six days, on admission, was profoundly septic, gums and lips sloughing, teeth dropping out, eyes injected and excreting profusely, cervical nodes much swollen, patient unconscious. He was given 50 c.c. of antistreptococcus serum on the second day after admission to the hospital, when his temperature was 102.3 F., pulse 150, respiration 132. The subsequent course of his temperature and pulse is shown in chart 3.

Two days after receiving serum, the condition of the mouth and gums had very much improved. On the sixth it was noted that the patient was crying for food. On the eighth the pulse, temperature and respiration were normal and the recovery was complete.

CASE 7.—L. J. (Chart 4), aged 15, had been ill two days on admission; very toxic; vomiting was constant; throat was very much swollen, also the cervical nodes; pulse very rapid and feeble. Improvement took place in twenty-four hours, with uneventful recovery, after the administration of 100 c.c. of serum, given on the third day after her admission to the hospital.

CASE 8.—R. S. (Chart 5), aged 6½, ill two days. Dr. Sexton, who observed the case throughout, noted that the patient was wildly delirious, but did not regard her as septic. The temperature was 105.5 F., pulse imperceptible, respiration 44. She was given 50 c.c. of serum on her admission to the hospital; twenty-four hours later the delirium was less marked and the temperature and pulse were down. The following day the patient's condition was excellent, delirium had ceased, and recovery was very rapid.

CASE 9.—H. S. (Chart 6), aged 10, had been ill two days on admission. The patient was very septic, with swollen throat and cervical nodes. Fifty c.c. of serum was given on the fourth day of her illness. Temperature and pulse fell by rapid lysis, and recovery was uneventful.

These examples are sufficient to illustrate the apparent effect of the serum on the pulse and temperature, and on the general and local septic conditions.

In a number of other cases in which the temperature was not so high, but in nearly all of which the pulse was very rapid, the effect of the serum

was marked. The following illustrates its usefulness in local conditions about the nose and throat.

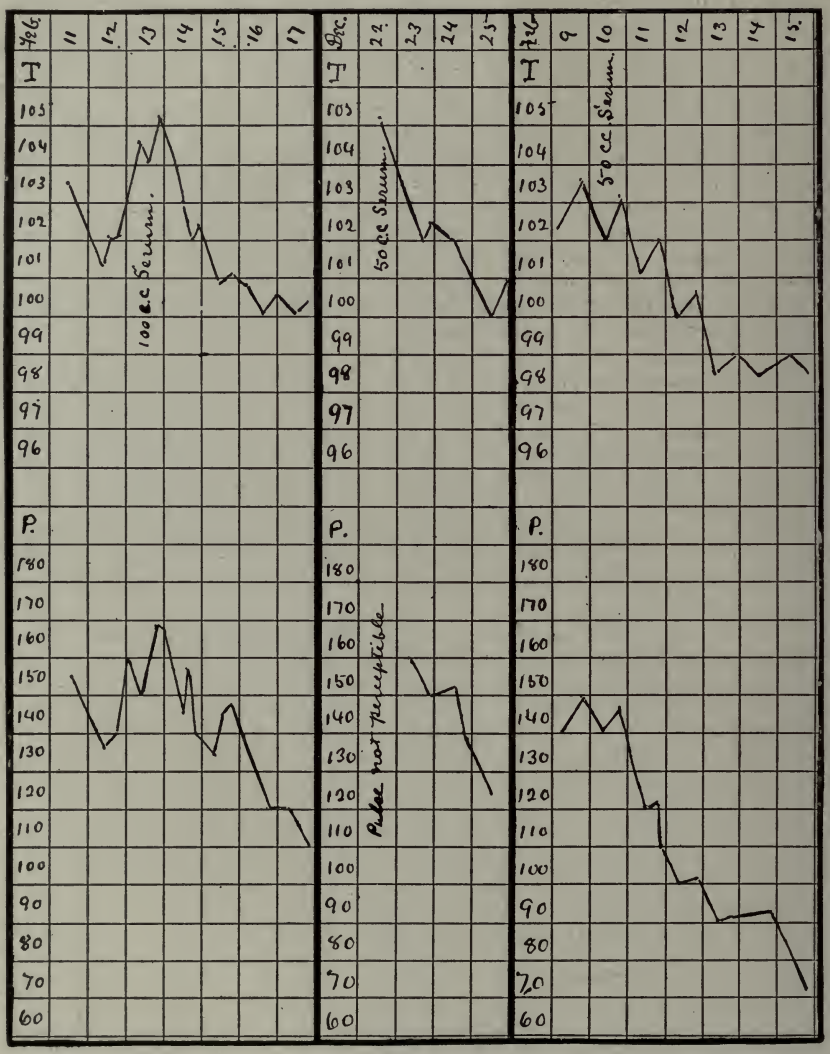


Chart 4. Chart 5. Chart 6.

Chart 4.—Effect of serum treatment in Case 7.

Chart 5.—Result of serum treatment in Case 8. Patient ill only three days.

Chart 6.—Showing drop in pulse and temperature after administration of serum in Case 9.

CASE 10.—S. K., aged 8½, had been ill five days on admission. The patient was apparently suffering from marked general sepsis, with profuse, foul, dark-colored nasal and oral discharge, with great swelling of the cervical nodes; lips also markedly swollen and fissured. The patient's mouth was wide open all the time. He was extremely apathetic. On the eighth day of his illness he was given 50 c.c. of serum, at which time the temperature was 101, the pulse 140. The amount of discharge from his nose and mouth was simply appalling. The temperature the next day rose 2 degrees; the pulse fell slightly. The following day the pulse fell to 110, the discharge showed very marked improvement and a few days later had ceased, the patient making an uneventful recovery.

What bad effects from the serum may be expected? In the foreign statistics rashes of various kinds occurred in a large number of cases, generally, however, of an urticarial type; also rise of temperature, evidently due to the same cause in about half the number, and occasionally polyadenitis, arthralgias and localized edemas. In my experience, I should say that with a dosage given subcutaneously, even of 50 c.c., an urticarial rash was the rule rather than the exception. Other and severer forms of rash I have not seen. A moderate rise of temperature accompanying the rash is not infrequent. Polyadenitis and arthralgias which could be definitely attributed to the serum were not noted. One case of true anaphylaxis occurred recently:

CASE 11.—P. P., aged 5, was admitted January 28, after one day's illness with scarlet fever and diphtheria. He was given 6,000 units of antitoxin on admission, and on the following day, as his throat seemed worse, 10,000 units. The patient had a tuberculous hip joint and was in generally poor condition. His subsequent history was that of chronic sepsis, with double mastoid infection, requiring operation, and abscesses in various parts of the body which when opened healed very badly.

April 17, seventy-nine days after admission to the hospital, a blood-culture was made and immediately antistreptococcus serum was allowed to run into the same vein. It ran very slowly, not more than 10 or 15 c.c. entering the vein, when the patient, who had been whimpering, gave one or two sharp coughs and attempted to vomit. The face became intensely cyanosed, and then deathly pale, except for a purple band extending across the forehead and eyes. The needle was immediately withdrawn, and the patient put to bed. He was unconscious, his color absolutely death-like; the pulse could not be felt; a dusky erythema covered the whole front of the body. The respirations, which had previously been 38 to 40, varied from 15 to 22 a minute with deep inspiration, very noisy and drawn through closed teeth. A few minutes later a purpuric rash covered the right limb from hip to ankle, the color disappearing only under long pressure. On the inside of the left leg, was a rash somewhat scarlatiniform in character.

These rashes disappeared in half an hour, except on the inner side of the right foot, where a circinate rash took the place of the purpuric. Under active stimulation and heat, consciousness returned within an hour and the patient recognized those about him. There were râles at the bases of both lungs which had not been noted previously. The next day the pulse, temperature and respirations were about as they were previous to the injection. On the following day there

was an exanthematous rash on the scalp, and a patch of erythema in front of the right ear. The subsequent history of the patient was one of progressive emaciation, death taking place about ten days later.

Whether these phenomena would have resulted from a subcutaneous injection I am unable to say. In another case, not scarlet fever, the patient developed a severe local anaphylaxis followed by an extensive area of sloughing at the point of inoculation following her eighteenth subcutaneous injection, the previous injections having caused nothing more than a mild urticaria. For this apparent lack of immunity to horse-serum, after seventeen injections given at short intervals, I have no explanation to offer, unless it is to be regarded as an example of the Arthus phenomenon. I have had an opportunity during the last few months to observe the effect of large doses of this serum given intravenously, and with the exception of the case mentioned I have not seen any alarming results which could be attributed to this method of administration. However, I am not prepared at this time to recommend its general use in this way, except in those cases in which a delay of twelve hours would probably determine a fatal outcome. Here, intravenous injections are by all means to be preferred.

Until there is some method of standardization and concentration of the serum, it would seem highly desirable to use a dosage believed to be essential to the best results by those who have had most experience with it, namely, for older children and adults, 200 c.c. injected, by preference, one-half into each side of the lower abdomen; for infants and young children, 100 to 150 c.c. in all.

The apparatus employed has been used for a number of years in the New York Department of Health for the inoculation of horses with large doses of serum, and I have found it most convenient for clinical purposes. It consists of a glass container, which may hold from 100 to 200 c.c., a rubber tube sufficiently long to be convenient, and a force pump which serves to give enough pressure to cause the serum to enter the tissues through the needle. It may be used equally well for intravenous injection. Care should be taken to see that the serum is heated to 100 F., otherwise a chill will result.

Finally, while my somewhat limited experience with this remedy does not entitle me to form a decided opinion, I cannot help but feel that in a disease over which we have little or no control, and which so frequently goes unexpectedly wrong, in all severe cases of scarlet fever, the serum, if attainable, should be made use of in full doses and without delay.

124 East Sixtieth Street.

THE THERAPEUTIC UTILITY OF DIPHTHERIA ANTITOXIN, WITH REMARKS ON ANAPHYLAXIS AND ON THE FEASIBILITY OF A SCRATCH TEST

AUGUSTUS CAILLÉ, M.D.
Professor of Medicine (Diseases of Children), New York Post-Graduate Medical School and Hospital
NEW YORK

Behring's great discovery of *diphtheria antitoxin,* which made its practical *début* in 1894, has revolutionized the treatment of diphtheritic infection; it has saved many lives and added much to the sum total of human happiness. Statistics show a lowered mortality of at least 50 per cent. in all kinds of cases, mild and severe. The experience of the individual physician is still more convincing than statistical figures. Whereas formerly he had the feeling of helplessness he now feels that the disease is under control if taken in time. Thus after seventeen years of practical experience with this therapeutic agent the civilized world has accepted diphtheria antitoxin as a true specific, both curative and protecting, but the mortality from diphtheria still remains higher than was predicted by Behring (5 per cent.) and higher than it should be if it has the curative power we attribute to it.

To my mind, the principal reason for the present day mortality in diphtheria, not taking into consideration the occasional and unexplained violent epidemics, lies in the fact that we do not sufficiently recognize the *great divergence of clinical manifestations of diphtheria* and, furthermore, that we have failed thus far to educate the general public along these lines.

Of all acute infections diphtheria and influenza stand first in their great divergence of clinical manifestations, and in order to get the best results and make the best use of a great remedial agent in diphtheria, we as a profession must know all phases of the diphtheria situation and should be willing to spread our knowledge into the public as much as feasible.

In this communication I will briefly present my personal viewpoint and experience regarding some of the clinical manifestations of diphtheria as we see them in New York and vicinity.

ANTITOXIN IN TONSILLITIS AND IN THE ORDINARY FORMS OF DIPHTHERIA

We need not take up much time discussing the usual forms of diphtheritic localization with which even the layman is familiar. Apart from such cases as show a tendency to relapse after first improving, the primary pharyngeal, tonsillar or laryngeal diphtheria cases show great uniformity in their behavior under repeated doses of from 3,000 to 5,000 antitoxin units. With good hygienic management and energetic and early specific treatment the mortality is not much over 5 per cent. But, if in the presence of a visible pseudomembrane or exudate we assume the ultra scientific attitude of waiting a day or two for a confirmative laboratory report before administering antitoxin, our mortality will be 12 to 15 per cent., and such indeed are the mortality figures for the states of New York and Pennsylvania in the last few years. The principle of giving the patient the benefit of the doubt is a safe and sane one in diphtheria as it is in syphilis, and, moreover, in the first mentioned acute infection no time is to be lost, and in the event of an unfavorable termination of a bad case we can bow to the inevitable without regret or reproach.

Let me illustrate this point by drawing the attention to the clinical behavior of so-called tonsillitis in our large cities.

If we look into the throat in a case of so-called follicular tonsillitis we see an inflamed large tonsil with white dots (not patches). That according to the text-books is tonsillitis, which should subside in a few days under non-specific management. But what we frequently observe in such cases is, that on the occasion of our second visit and inspection, we find that some of these spots have coalesced to a small patch, and subsequently to a large patch, with all symptoms of diphtheritic sepsis. The experienced practitioner knows that it is often impossible to *distinguish clinically between tonsillitis and diphtheria*, and that it is unwise to wait for a confirmatory laboratory report before giving antitoxin. Whenever we observe sore throat in a child with fever and swollen lymph nodes, be the lesion ulcerative or exudative, antitoxin is promptly indicated. The fear that a family or community will be needlessly alarmed by a call for antitoxin in cases in which the laboratory report is subsequently negative must not deter us from using this remedy in good time, particularly if we emphasize its prophylactic virtues in doubtful cases. All this is old history, but it emphasizes the fact that the rank and file in our profession do not up to the present time make the best use of diphtheria antitoxin.

NASAL CATARRH AND PRIMARY NASAL DIPHTHERIA

When the writer first went to school in a little log house on the bank of the Mississippi, in Iowa, in 1861, most every boy and girl had a running nose in the winter. No doubt some had adenoids or other nasal obstruction and occasionally all had so-called "colds," with a thick, whitish discharge from the nostrils frequently associated with a croupy cough. Diphtheria had not penetrated to our region, and running noses subsided in due time.

Now what do we frequently observe at the present day in New York City? A running nose, usually one-sided; a thin, blood-colored, greenish discharge; an excoriated upper lip; perhaps a week later a croupy cough is noticed and stridulous breathing, and finally stenotic breathing and cyanosis. *During all this time the pharynx is free from pseudomembrane, and pale in appearance.* The experienced colleague recognizes the clinical picture of primary nasal diphtheria at an early stage, and extinguishes the smouldering flame with a few doses of antitoxin. The clinical novice may or may not apply the remedy when it is all but too late, although in primary nasal diphtheria he has ample time to wait for a laboratory report before administering specific treatment.

ANTITOXIN IN SCARLET FEVER AND MEASLES

When scarlet fever or measles is complicated by diphtheria *from the start,* we usually have to deal with a severe double infection which is occasionally fatal in spite of early energetic treatment. In such cases it is extremely unwise to wait for a confirmatory laboratory report, because one or two harmless doses of antitoxin will assuredly counteract a part of the sepsis and may turn the tide in favor of the patient. In measles with so-called follicular tonsillitis a subsequent laryngeal stenosis is not infrequently observed and should be promptly forestalled by the administration of antitoxin.

In measles and scarlatina, diphtheria is often a complicating feature *after the skin eruption has subsided.* Such cases are not as severe as the simultaneous double infection, and here the antitoxin need not necessarily be administered until throat symptoms are really in evidence.

ANTITOXIN IN SOME FORMS OF BRONCHOPNEUMONIA

It is not generally appreciated that certain forms of bronchopneumonia and pleuropneumonia can be favorably influenced by diphtheria antitoxin.

An apparent *primary diphtheritic bronchopneumonia* is an occasional occurrence in adults as well as in children. The clinical features of this variety of bronchopneumonia differ somewhat from the simple, the syphilitic, the tuberculous, or the influenzal varieties, inasmuch as an early and persistent subjective and objective dyspnea with pronounced cyanosis are much in evidence. Not infrequently large and shreddy membranes are coughed up, the voice is usually husky, hoarse and croupy. Whenever a primary or secondary diphtheritic bronchopneumonia is suspected antitoxin should be administered freely and under circumstances in large doses; at the same time 5-grain doses of camphor in oil should be given every two hours for a period of one day. This variety of bronchopneumonia is frequently fatal, but recoveries under specific treatment have been observed and reported.

ANTITOXIN IN WHOOPING COUGH AND DIPHTHERIA

Whooping cough may be complicated by a visible throat diphtheria or by membranous croup with a free pharynx. The congested condition of the upper respiratory tract in pertussis favors diphtheritic infection. Therefore, antitoxin is indicated as soon as the slightest visible throat or nose exudate or membrane is in evidence, and in the event of a *croupy cough* in pertussis, the prompt administration of antitoxin is life-saving, inasmuch as it usually makes intubation unnecessary, for it is well known that intubation in children weakened by severe spasmodic cough is usually followed by severe bronchopneumonia which may end fatally in young children, in spite of the best management. In some cases a careful observer will find the whooping-cough blisters (stomatitis) in the mouth of the child covered with a dense pseudomembrane, several days before the croup symptoms are in evidence and will promptly administer antitoxin in order to limit or overcome the spread of the exudative inflammation.

ANTITOXIN IN STOMATITIS AND NOMA

We all have seen ulcerative stomatitis and noma (gangrene) with extensive destruction of tissue. Such cases impress us clinically as the analagon of phagodenic chancres. It is quite natural, inasmuch as these lesions usually begin somewhere on the buccal surface, that we should look for diphtheria bacilli in these cases, suspecting a mixed infection. But such cases usually run their course with culture findings negative as to diphtheria. Notwithstanding this well-known clinical fact, it is wise to give a few doses of antitoxin in such cases, first on general principles

and because there are cases on record in which improvement set in as soon as diphtheria antitoxin was administered.

ANTITOXIN IN FOUL SMELLING SORE THROAT AND MOUTH WITH A PUS-LIKE NON-MEMBRANOUS EXUDATE

Two cases of this variety of sore throat recently came under my observation. A girl of 12 first took sick, then her brother of 5. The pharyngeal exudate was pus-like, the laboratory report was staphylococci. No diphtheria bacilli. The girl became rapidly anemic and too weak to sit up. Local measures, stimulation and the administration of the tincture of chlorid of iron gave no improvement. In the third week 3,000 antitoxin units were administered every other day, altogether three doses, whereupon rapid improvement was noticed.

The younger child after being ill in the same way for a week, developed croup and progressive stenosis, and was well after five doses of antitoxin, each 3,000 units. Here also a culture was negative as to diphtheria bacilli.

Such cases seem to bear out the contention of those investigators who claim positive therapeutic virtues for diphtheria antitoxin in certain non-diphtheritic ailments.

ANTITOXIN IN MISCELLANEOUS FORMS OF DIPHTHERIA

Pseudomembranous conjunctivitis is not, as a rule, diphtheritic but it may be. This is also true of ulcerative and suppurative keratitis. In all positive or doubtful cases antitoxin is indicated.

Cases of puerperal sepsis with a visible pseudomembrane on the labia or deeper parts should receive one or two injections of antitoxin without waiting for a laboratory report.

Cases of facial erysipelas following tonsillar diphtheria have been observed and should receive specific treatment.

Diphtheritic enteritis with a passing of large membranes and well-defined postdiphtheritic paralysis have been reported.

Wound diphtheria, especially after operation on the nose and throat, is not a rare occurrence.

Adenoid vegetations may also be the primary seat of a diphtheritic process. For bacteriologic examination, the material in such cases must be taken from behind the soft palate or through the nose.

In all these miscellaneous forms of diphtheria, antitoxin is indicated.

ANAPHYLAXIS (HYPERSUSCEPTIBILITY)

A discussion of the therapeutic utility of diphtheria antitoxin would be incomplete without a consideration of the biological phenomenon known as anaphylaxis. When albuminous substances are introduced into the circulation other than by the way of the gastro-enteric tract (by subcutaneous, intraperitoneal or intravenous injection) immune bodies are formed in the blood and the individual becomes sensitized for the specific proteid injected and for an indefinite time period but *not for any other form of protcid.* This process is best illustrated by citing the sugar experiment. If grape sugar is injected into the vein of a guinea-pig an immediate decomposition of the injected sugar does not take place. But soon thereafter a grape sugar splitting enzyme is formed in the blood, and a subsequent second injection of grape sugar is immediately reacted on by this previously formed enzyme. In a similar way if an albuminous substance be injected into the vein of a guinea-pig an enzyme is formed and thus a second injection of proteid two weeks after the first will be reacted on the enzyme and the albuminous substance *will be peptonized in the circulation,* giving toxic anaphylactic symptoms similar to those observed when a peptone is injected directly into the veins of a non-sensitized guinea-pig.

This is known as an *albumin peptone reaction,* and in anaphylaxis this peptone reaction is *specific for a specific variety of albumin and for none other.*

If we inject subcutaneously 0.01 c.c. of horse serum into a guinea-pig and after two weeks 1 c.c. of human serum, no reaction will follow. If thereupon we inject 1 c.c. of horse serum, the animal becomes *anaphylactic.* Within half a minute it will scratch its nose, its hair will rise, fibrillary twitchings will be observed and the animal becomes comatose. Within two to three minutes severe tonic and clonic convulsions will set in and end in death. When this anaphylactic shock is too weak to kill, the rectal temperature of the animals sinks from 38 to 36 or 30 C. within the next eight to fourteen days, and no specific reaction in cases of recovery will follow a renewed injection of horse serum (*anti-anaphylaxis*). This well-known fact has been utilized in practice. Human beings who show extreme sensitiveness to serum antitoxin have been safely brought under its influence by beginning with minute doses and gradutlly increasing the dose.

When guinea-pigs have succumbed to anaphylactic shock the lungs are found pale and distended. They fill up the entire thoracic cavity and do

not collapse, as though under the control of bronchial spasm. The heart pulsates for from five to forty minutes after apparent death.

These severe toxic anaphylactic phenomena have been observed so far only in guinea-pigs. In rabbits, cats, dogs, chickens, human beings, a mild form of anaphylaxis has been reported, but not as yet sufficiently studied.

A SCRATCH TEST

Primary serum antitoxin injections in the acute stage of diphtheria in human beings are, as experience has shown, harmless. The degree of sensitiveness to serum administered to a *sensitized individual* varies, according to the writer's experience, in different individuals. At no time has he observed serious results following the administration of serum to an already sensitized patient. In a limited number of cases in which the writer has injected antitoxin on various occasions and years apart in the same individual, a violent erythematous eruption extending over the entire body was observed, but never a fatal result. As a possible safeguard for individuals previously sensitized by horse serum the writer has used and suggests the use of a *scratch test.* This test is made in the same way as the v. Pirquet test for tuberculosis. If a minute quantity of serum rubbed into a scratch in the skin should be followed by a severe local or systemic reaction, its further introduction into the system in the full therapeutic dose would be contra-indicated. Moreover, it would seem important to employ in already sensitized persons an antitoxin *derived from some other animal than the horse, or an antitoxin disassociated from albumin, if that were possible.* The writer's experience with the *scratch test* is as yet too limited to permit of a statement as to its definite value.

ANTITOXIN AS A PROPHYLACTIC

Until the question of anaphylactic shock in human beings is definitely settled, immunizing injections of serum should be resorted to only for the purpose of limiting an epidemic or for protecting exposed individuals who cannot be protected by isolation; or better still, *immunizing injections should be made with a serum other than that which comes from the horse.* When the immunizing power of diphtheria antitoxin is invoked, the time lost in first making a bacillary inquiry is not a serious matter.

The induction of an active immunity in the human being by means of repeated injections of minute doses of *diphtheria toxin* has also been accomplished, but it is too early to discuss the feasibility of this procedure from a clinical viewpoint.

RÉSUMÉ

The scope of the application of diphtheria antitoxin may be considerably widened in non-sensitized individuals.

For detecting hypersusceptibility to serum preparations in their parenteral application to sensitized persons, a *scratch test* is suggested.

In view of anaphylactic phenomena observed and reported, the administration of serum preparations to *sensitized persons* requires further study.

DISCUSSION

DR. GRAHAM: Recently in the preparation of a paper on diphtheria I had occasion to look up the subject of anaphylaxis. In the Widener Memorial Hospital for Crippled Children the patients are apt to remain for a long time. Occasionally, in spite of all the care that can be taken, a case of diphtheria will gain admission and it has been the practice there for a long while to give an immunizing dose of antitoxin. That rule has brought it about that many children in the institution have had, at varying periods of six months or a year, doses of 1,500 or 2,000 units and over a long period of years no injurious effects have been observed. I took up this subject of anaphylaxis at the Municipal Hospital in Philadelphia also and there they have records of children readmitted two or three times and they have never in their large experience, covering years, seen any evidence of anaphylaxis, of any but a very mild degree. It seems to me rather important for us to decide definitely whether or not there is any real danger from anaphylaxis, and if so just how great the danger is. The possibility of our influencing physicians against the use of antitoxin by preaching anaphylaxis may be very considerable, and if in these two institutions, where thousands of children have been treated and where there have been hundreds of repeated injections, nothing but trivial symptoms have been observed, it seems to me we can ignore anaphylaxis as a danger.

DR. PISEK: I think in the discussion of this subject of anaphylaxis we must bear in mind what constitutes a foreign albumen. Any serum taken from one species of animal and injected into another species is a foreign albumen; it is not even necessary that this substance be a serum, for a reaction may be brought on with egg albumen, with milk, etc. Hypersusceptibility may be primary, e. g., inherited or attained accidentally. A natural or accidental hypersusceptibility to horse serum is not unknown, and in these cases the first injection of antitoxin may cause a severe anaphylactic shock. If injections are repeated we, of course, are very apt to get such a reaction, which may be so severe as to threaten life or so mild as to hardly be noticed. As to the scratch test, very minute quantities of the protein would cause a local anaphylactic shock and it would be almost impossible not to introduce in this manner enough protein to cause such a reaction. If we had such a test available it would be helpful; but at the present time it seems to me that we should use antitoxin freely in true diphtheritic cases, but not in those cases which are simply spasmophilic in type. Unless the patient is susceptible, there is no anaphylaxis. Langerhans has recently reported an instance of a young man who could not go near a horse without having asthma and who on being injected with horse's serum almost succumbed. The manner in which such a condition is brought about is difficult of explanation; though we know that very minute quantities of protein will

produce hypersusceptibility in guinea-pigs, and may from analogy conclude that a like condition may rarely occur in human beings.

DR. KNOX: I have been interested in the suggestion of the scratch test as a means of opening our eyes to the possible effect of a subsequent injection of horse's serum. We find in rabbits that we can get a reaction, with all the local skin signs, and that the reaction can be modified by an injection of a strong oxidizing substance. This can be done to some extent with dogs. On the other hand, when given in large quantities this substance doesn't prevent the tremendous drop in blood-pressure; i. e., does not affect the systemic anaphylactic reaction. It seems to me, therefore, that the skin reaction is one of those processes closely related to anaphylactic shock but somewhat different from it. So that I doubt very much whether, if one did find that the patient was susceptible to the skin reaction, that would be a very definite indication that he would not be susceptible to a subsequent injection of horse's serum.

DR. SNOW: I agree with Dr. Pisek that antitoxin should not be used without definite symptoms. I had a sore throat and was given 3,000 units. Three years afterward I was exposed and was given 1,500 units. Three days after this there appeared an erythema and urticaria, which lasted thirty-six hours and which was only relieved by a hypodermic of atropin. I feel that I would rather have diphtheria than another dose of antitoxin.

DR. NICOLL: It seems to me it would be a great mistake to let the idea of a possible anaphylaxis interfere with our use of antitoxin as a preventive against diphtheria. I would add two other institutions to the list of those in which there has been no such trouble. At the New York Foundling Hospital the children receive 1,000 units. Dozens and dozens of them have received more than one dose and there has never been a case of anaphylaxis. At the Scarlet Fever Hospital and Diphtheria Hospital of the Department of Health the physicians have never seen anything of the kind. It would appear that the fear of anaphylaxis is being overworked. We are getting a little hysterical on the subject.

DR. KERLEY: At the Nursery and Child's Hospital we have diphtheria more or less during the entire year. At this institution all sorts of children are admitted regardless of their former associations. This means that more or less contagion slips in. When diphtheria develops in a ward the child is removed and all the other children get from 500 to 1,000 units of antitoxin for immunization purposes. In perhaps a few weeks or months another case develops and again the children are immunized. Some of the children get repeated injections and we have never seen any evidence of anaphylaxis. It would seem that there can be no great danger in the repeated use of antitoxin. Before we take any definite stand in such an important matter that might influence the general practitioner, we should know a great deal more about it.

DR. RUHRÄH: I agree with Dr. Kerley that it would be a great mistake to lay too much stress on this idea of the danger of anaphylaxis, as a great many physicians are already afraid to use immunizing doses of antitoxin, and it is very important not to scare the general practitioner about the use of an agent of such great value.

DR. EATON: I fully agree with the last two speakers because my own experience has been the same as theirs. We use the antitoxin in this way and have never seen a single case of anaphylaxis. I have used it in fifteen cases of scarlet fever, in the beginning, cases with bad throat conditions, and have

seen the attack end by crisis. It seems to me there is something in it that we do not as yet completely understand, and we should be very cautious about saying anything against its use where it would seem that it may do good.

DR. CAILLÉ: In closing the discussion I would simply say that I will let my paper stand as read. Let us all combine in an effort to get at the real truth concerning anaphylaxis and report again next year. If there is anything new to learn about serum therapy let us lose no time.

THE TREATMENT OF PERTUSSIS WITH VACCINE

EDWIN E. GRAHAM, A.B., M.D.
Professor of Diseases of Children, Jefferson Medical College.
PHILADELPHIA.

The seriousness of pertussis in the infant, its tendency to be complicated by pneumonia, emphysema, convulsions and perhaps paralysis, and the possibility of a fatal termination, have caused this disease to occupy a prominent place in the minds of all physicians, particularly as it is so commonly seen in infancy, 50 per cent. of all cases occurring in the first two years of life. As the treatment of pertussis by drugs is so unsatisfactory, it is important that any new treatment that offers a reasonable hope of success should be thoroughly tested.

Pertussis is undoubtedly contagious and positively due to a micro-organism, and it seems to me that the bacillus described by Bordet and Gay in "Studies in Immunity" has many claims to the position of the specific pathogenic organism.

Bordet and Gengou[1] claim to have found the true bacillus of pertussis. They assert that the bacillus is found only in the early period of the disease, and only that part of the expectoration which comes from the region in which the bacteria are most active should be used; i. e., "the products from the depths of the bronchi, expectorated during the periodic accesses of the disease." This exudate contains the true bacillus in considerable numbers and, in favorable cases, in almost pure culture. "As the disease progresses, on successive days fewer and fewer specific bacilli are found and phagocytosis is more frequent than earlier." They emphasize the importance of studying cases not complicated with other respiratory affections, and of avoiding the study of the sputum of hospital patients, as in the latter other organisms are apt to be present in great numbers.

They describe the micro-organisms of pertussis as "little ovoid bacilli, somewhat elongated at times, but frequently so short as to resemble a micrococcus." With Kuhne's carbolated blue stain, the bacilli will stain a pale blue, and the outline of the bacillus, and particularly its

1. Bordet and Gengou: Studies in Immunity, 1906, chap. xxvii.

poles, are frequently more deeply stained than the center. "This organism was found scattered indiscriminately among the cells and was at times within cells." It was negative to Gram's stain.

This bacillus does not grow well on blood-agar. It develops well in a liquid medium of 1 per cent. glycerinated bouillon with equal parts of rabbit's blood or serum. It is found that the organism grows only under the best condition of aerobiosis.

"The authenticity of this bacillus as the causal agent in whooping-cough rests in large part on the circumstances in which it is found, namely, the excessive growth of the organism in pure culture during the initial period of the disease in young children who have never been ill. The principal argument, however, in favor of the organism appears to be furnished by a study of the specific properties of the serum. The serum of individuals who have never had whooping-cough, or who have had it a long time before, does not agglutinate the bacillus even in low dilution. The serum of children who have recently recovered from the disease has a moderate agglutinating property which is constant and evident. The most remarkable fact, however, is the intensity of the sensitizing property in such serums."

Bordet and Gengou assert that the organism described by Pfeiffer resembling the influenza bacillus, "acts no differently with whooping-cough serum than it does with normal serum." They find that the serum of children suffering from, or convalescent from whooping-cough, shows very inconstant agglutinating properties. An agglutinating property in a mild form is frequently present; it may be entirely lacking. They find, however, that the alexin fixation method always gives marked positive results.

Bordet, as described in a later communication (1908), has obtained from the organism an endotoxin. He and his coworker hope to obtain an antitoxic serum by injecting endotoxin instead of bacteria, and claim that the bacillus produces a poison that causes a necrosis of that portion of the epithelium covering the bronchi where rapid increase in the number of the bacilli occur, and that this necrosis is the cause of the characteristic symptoms of pertussis and their persistence.

As I was without any previous knowledge of the amount of vaccine to administer and was consequently ignorant as to the number of bacteria to inject, my earliest patients received only 20 million bacteria every four days. This dose failed to produce any untoward symptoms locally or constitutionally, and was increased to 40 million bacteria every four days. A careful study of the patients receiving this dose, by all those coming in contact with the patients, including parents, other physicians and myself, tended to show that the disease was apparently being modified

by the treatment. The same dose was then given every three days, and the beneficial results seemed to be distinct. The number of paroxysms of coughing became less; the severity of the paroxysms diminished, cyanosis was less marked, vomiting during the coughing was less frequent, and the children, as a rule, slept better and were less disturbed at night, since the number of characteristic attacks became less. The dose of 40 million was retained, but the injection was now given every two days. The number of injections given varied from six to eight. No case has been recorded in which less than six doses were administered, and none of the patients received more than eight injections of 40 million each, except twenty-two, who had nine injections. In not a single instance were evidences of local inflammation noticed at the site of the injections, and while most of the injections were given in the loose tissues of the scapular region, some children received injections into the arms.

The interscapular region is, in my judgment, the best place for injection, as it is difficult for the child to scratch this portion of the body, and it is apt to be fairly well protected by clothing. Care was taken to render the part injected clean with soap and water and alcohol and to sterilize the hypodermic syringe. Neither I nor any other physician to whom I gave the vaccine noticed any local or constitutional effects from the remedy; rashes, joint pains and fever were carefully looked for, but were never observed.

All but one of the cases were in private practice, and this affords a much better test of the efficacy of the remedy than a study of hospital cases. Institution children in whom whooping-cough develops while in the ward, are immediately sent to the pertussis pavilion, and are apt, therefore, to be in intimate contact with other pertussis patients, who may have other infections of the respiratory organs. Moreover, institution children do not, as a rule, do well when attacked by infections, and are therefore less apt to show the true beneficial effects of which a remedy is capable. I do not wish to be understood as suggesting that it should not be used on hospital patients, but they are manifestly less apt to exhibit the true influence of the remedy, as they are, as a class, less vigorous and robust than children living outside of institutions. This, of course, applies more to children under 2 years of age. Older children are less apt to be affected with hospitalism. Outside children admitted to hospitals with pertussis are apt to be received late in the disease and commonly have some complication, often pneumonia. I would strongly advise that all these children be given the benefit of the vaccine treatment;

I believe that a thorough trial of it in these cases will demonstrate its efficacy; but for the purpose of this investigation and study, private cases are better.

Physicians are apt to be too optimistic in ascribing to new drugs or methods of treatment curative properties. A more extended trial may prove their conclusions to be premature and unfounded, and this may be the fate of pertussis vaccine. In order at least partially to eliminate this error, those coming in intimate, daily contact with the patients, parents, nurses and other members of the household, have been systematically questioned, and their opinions, in the large majority of cases, have been in favor of the remedy — that it tends to diminish the severity and number of the attacks and shorten the course of the disease.

After the injections were stopped, the cases were followed as closely as possible to see whether the usual course of the disease was influenced only during the use of the remedy, and whether the paroxysms of coughing would return after the discontinuance of the vaccine. This method of following the cases resulted in showing that improvement almost invariably continues steadily after the course of treatment by the vaccine has been discontinued.

It is, of course, well known that epidemics of pertussis differ greatly in their severity, and it may be that future cases will be less influenced by the treatment than those cases on which this paper is based. I have seen personally many of these cases, and in my judgment they were cases of ordinary severity. In the list of cases here reported, no child was included who did not have the typical whoop, and this typical whoop was heard by the attending physician in each instance. The judgment of the parents or nurse was never taken on this point.

In all, twenty-four cases of pertussis are reported. The ages of the children were as follows:

	Cases
Less than six months	3
6 months to 1 year	2
1 to 2 years	4
2 to 4 years	10
4 to 8 years	5

REPORT OF CASES

CASE 1.—Mary H., aged 3 years, colored, pertussis ward, Philadelphia Hospital; first injection given March 14, 1911; whooping two weeks before treatment began; received six injections, three of twenty million, three of forty million. A careful systematic daily record was kept of the number of the paroxysms in every twenty-four hours, of the duration in minutes and seconds of each

paroxysm, whether severe, moderate or mild, and the frequency of vomiting produced by the paroxysms of coughing. Careful records of the temperature, pulse and respiration were recorded only in those cases in which there was fever. The record shows that the child was much benefited by the treatment. The paroxysms were reduced from an average of twenty in twenty-four hours to five in twenty-four hours. The duration of the paroxysms was much shortened. They were less in severity, and the frequency of the vomiting attacks diminished. The temperature, respiration and pulse all improved. From March 14 to 20 the temperature varied from 101.5 to 100 F.; March 21 to 28, 101 to 100 F.; March 28 to April 1, 100 to 99 F.; April 1 to April 8, normal.

There is no doubt in my mind that the child was distinctly benefited by the treatment. The records kept in the hospital are too voluminous to publish. However, the portion of the record here is of interest.

HOSPITAL RECORD OF MARY H.

Admitted to whooping cough isolation ward March 1, 1911. Received vaccine lymph (pertussin), 20,000,000, March 14, 1911.

First dose March 14: March 14, 4 p. m., to March 15, 4 p. m., total number of times coughed, 18; coughed hard 14 times; vomited, 7 times; coughed not so hard, 4 times; expectorated, 7 times.

March 15, 4 p. m., to March 16, 4 p. m., total number of times coughed, 12; coughed hard 5 times and vomited; coughed hard 7 times and expectorated.

March 16, 4 p. m., to March 17, 4 p. m., total number of times coughed 11; coughed not so hard, 4 times; coughed hard, 4 times; coughed hard and vomited, 3 times.

Second dose, March 17: March 17, 4 p. m., to March 18, 4 p. m., total number of times coughed, 10; coughed not so hard, 4 times; coughed hard, 3 times; coughed hard and vomited, 3 times.

March 18, 4 p. m., to March 19, 4 p. m., total number of times coughed, 13; coughed hard and vomited, 6 times; coughed hard, 7 times.

March 19, 4 p. m., to March 20, 4 p. m., total number of times coughed, 11; coughed hard and vomited, 5 times; coughed hard 6 times.

Third dose March 20: March 20, 4 p. m., to March 21, 4 p. m., total number of times coughed, 8; coughed not hard, 4 times; expectorated; coughed hard, 4 times, vomited.

March 21, 4 p. m., to March 22, 4 p. m., total number of times coughed, 8; coughed not hard, 4 times; expectorated; coughed hard, 4 times; vomited.

March 22, 4 p. m., to March 23, 4 p. m., total number of times coughed, 9; coughed not so hard, 4 times; coughed hard, 5 times; vomited 4 times.

Fourth Dose, March 23: March 23, 4 p. m., to March 24, 4 p. m., total number of times coughed, 8; coughed not hard, 3 times; coughed hard, 5 times; vomited 3 times.

March 24, 4 p. m., to March 25, 4 p. m., total number of times coughed, 6; coughed not hard, 2 times; coughed hard, 4 times; vomited 3 times.

March 25, 4 p. m., to March 26, 4 p. m., total number of times coughed, 6; coughed not hard, 1 time; coughed hard, 5 times; vomited 3 times.

Fifth Dose, March 26: March 26, 4 p. m., to March 27, 4 p. m., total number of times coughed, 6; coughed not hard, 3 times; expectorated; coughed hard, 3 times; vomited.

March 27, 4 p. m., to March 28, 4 p. m., total number of times coughed, 6; coughed not so hard, 3 times; coughed hard, 3 times; vomited 2 times.

March 28, 4 p. m., to March 29, 4 p. m., total number of times coughed, 5; coughed not so hard, 1 time; coughed hard, 4 times; expectorated 4 times; vomited 1 time.

Sixth Dose, March 29, 4 p. m., to March 30, 4 p. m., total number of times coughed, 5; coughed not hard, 2 times; coughed hard, 3 times; vomited 2 times; expectorated 3 times.

March 30, 4 p. m., to March 31, 4 p. m., total number times coughed, 5; coughed not hard, 1 time; coughed hard, 4 times; expectorated 3 times; vomited 2 times.

March 31, 4 p. m., to April 1, 4 p. m., total number of times coughed, 8; coughed not hard, 3 times; coughed hard, 5 times; vomited 3 times.

April 1, 4 p. m., to April 2, 4 p. m., total number of times coughed, 6; coughed not hard, 1 time; coughed hard, 5 times; vomited 3 times.

CASE 2.—Elizabeth H., aged 3 years and 10 months; report by Dr. E. D. Grier; treatment began April 11, 1911. The child had been coughing and whooping several weeks before the first dose of pertussis vaccine was given. She received five injections of twenty million and three of forty million each. The attack was of moderate severity. The child was much improved at the end of the treatment. The cough was almost gone and there was very little whoop.

The following is a brief résumé of the notes kept by the mother, a very intelligent woman.

April 11, 1911.—From 6 to 12:15 a. m. had coughed ten times; vaccine given at 12:15; coughed five times from 12:15 until 8 p. m.; vomited twice slightly.

April 12, 1911.—Coughed once during the night; coughed four times from 6 a. m. until 12 M.; vomited once; coughed three times from 12 M. until 6 p. m.; in all eight paroxysms.

April 13, 1911.—Coughed twice during the night; coughed four times during the morning, and four times during the afternoon; no vomiting.

April 14, 1911.—Coughed once during the night; no vomiting; coughed seven times during the day; appetite good.

April 15, 1911.—Coughed once during the night, about 5 o'clock; coughed seven times during the day; vomited once after taking 10 ounces of milk. Dr. Grier administered vaccine at 10 a. m.

April 16, 1911.—Coughed once during the night about 5 o'clock, but not since 4:30 the previous evening; seven times during day. Vomited once slightly.

April 17, 1911.—Coughed six times; vomited most of the first bottle of milk at 6:30 a. m., but ate a good breakfast. She takes a nap every morning of 1½ hours; seems much improved. The worst coughing spell is in the morning when she has some trouble in bringing up the phlegm.

April 18, 1911.—Coughed early in the morning; seven times during the day, and vomited a very small amount in the afternoon. "Severe cough at 3:30 p. m., while I was present."—Grier.

The baby received the last dose of vaccine May 6, and under this date Dr. Grier writes me as follows: "The family feel that the child is much improved, and the attack I heard to-day bears out their statement, as it was of no moment; the cough now is almost nothing."

CASES 3 AND 4.—Edwin W. and Kenneth W., brothers, aged 7 years and 4 years; first injection of pertussis vaccine April 11, 1911. Each received eight injections of forty million. Both had been whooping about one week before the treatment began. Both were benefited by treatment, the older boy more than the younger. In both children the number and severity of the paroxysms dimin-

ished. The younger boy had adenoids and tonsils removed May 20, six weeks after the beginning of the vaccine treatment. He was so much better that we did not hesitate to place him in a private room in a hospital for the removal of his adenoids and tonsils.

CASE 5.—William N., aged 15 months; first injection of pertussis vaccine May 10, 1911; whooping five days before treatment began; received eight injections of forty million each. After the sixth injection the child had a slight broncho-pneumonia; temperature varied from 101 to 103 F. in five days. The vaccine treatment apparently did not affect the pertussis in any degree whatever. The patient in my opinion was not benefited by the treatment. At the end of the treatment the boy was still coughing and whooping, but neither the cough nor the whoop was severe in character and the boy's temperature was normal. I believe that the dose in this case was insufficient to produce an effect. Instead of forty million, he should have been given at each dose eighty to 100 million.

CASE 6.—Francis N., 2½ years old, sister of Patient 5; first injection of pertussis vaccine May 10, 1911; whooping two weeks when treatment began. A severe case; numerous paroxysms day and night; vomited frequently, and often during attack became cyanosed; eight injections of forty million each were given. The paroxysms of coughing after the child had received four injections were distinctly less severe, although not diminished in number. After receiving the full number of injections, eight, the boy was much improved. The paroxysms were few in number, and very light, with only an occasional whoop.

CASE 7.—Isabella L., aged 4 months; whooping two weeks before treatment began; eight injections of forty million each were given; much improved; very little cough and occasional whoop. This child had a mild attack of pertussis, and at the end of treatment was practically well. Very little cough remained and hardly enough whoop to designate it by that name.

CASE 8.—David L., aged 2 years; first injection of pertussis vaccine May 12, 1911; whooping one week before treatment began; seven injections of forty million each were given. A careful record of the number and severity of the attacks was made. In the early part of the treatment the attacks were very severe; thirty-six in twenty-four hours. At the end of the treatment the attacks averaged about twenty-eight in twenty-four hours. There was no decrease in the severity of the attacks. The patient was apparently not benefited by the treatment. The case was reported by Dr. W. S. Lucas. I believe the dose of vaccine used in this case was too small. In a similar case I would advise eighty million or 100 million with each injection.

CASE 9.—Charles L., aged 8 years, brother of Patient 8; first injection of pertussis vaccine May 10, 1911; whooping ten days before treatment began. This was a much milder case than that of his brother, David L., Case 8. Patient 9 received eight injections of forty million each. At the beginning of treatment, he averaged fifteen paroxysms in twenty-four hours, moderately severe in type, about five or six attacks occurring at night. At the end of treatment he averaged about six or seven attacks in twenty-four hours, very mild in character, and not more than one or two at night. The boy was evidently much improved by treatment. Reported by Dr. W. S. Lucas.

CASE 10.—Fanny C., colored, aged 5 months; first injection of pertussis vaccine given May 5, 1911; a sturdy child, breast-fed, always in good health until the attack of pertussis. Paroxysms occurred every hour during the day and three or four times at night, vomiting with almost every paroxysm; face became deeply

congested with each attack of coughing. Six injections of forty million each were given; there was so much improvement at the end of the sixth injection that the mother considered the child well and wished the treatment discontinued. The child still coughed and whooped occasionally, but the paroxysms were very mild.

CASE 11.—Male, aged 5½ years; reported by Dr. S. M. Wilson; whooping one week before treatment began; eight injections—three of twenty million, four of forty million and one of sixty million; first injection April 29, 1911. Dr. Wilson wrote me as follows: "At the time of his first injection, he had twenty or more severe paroxysms daily and his sleep at night was badly disturbed by them. At the end of the treatment he rarely coughs, and when he does, there is usually only a single effort and no expectoration." Dr. Wilson considered that the boy was very much benefited by the treatment.

CASE 12.—Cecil D., aged 3 years; first injection of pertussis vaccine May 5, 1911; reported by Dr. H. W. Gregory. The child had been whooping three weeks before treatment began. The attacks were severe, occasionally producing hemoptysis; eight injections of forty million each were given. At the end of the treatment the child was practically well, averaging only one mild paroxysm during the night and with very little cough during the day.

Cases 13, 14, 15, 16 and 17 all occurred in the practice of Dr. S. M. Cleveland, and according to Dr. Cleveland's observations the patients were apparently not benefited by the treatment. The only explanation that I am able to give for the failure of the treatment in these cases is that the dose of vaccine used was not large enough. A brief history of these cases follows:

CASE 13.—Carl O., 16 months old, whooping five days when treatment began; seven injections of forty million each produced apparently no benefit.

CASE 14.—Dorothy O., sister of Patient 13, aged 4 months; whooping seven days; given seven injections forty million each; apparently no benefit from treatment.

CASE 15.—Elizabeth O. B., 10 months old, sister of Patient 16; coughing two months before treatment began; six injections of forty million each were given; apparently no benefit resulted from treatment.

CASE 16.—Marie O. B., aged 5 years; coughing for two months before treatment began; six injections of forty million each were given, with no benefit.

CASE 17.—James O. B., aged 7 years, brother to Patients 15 and 16; coughing two months before treatment began; six injections of forty million each were given, with no benefit.

CASE 18.—James L., aged 28 months; first injection of pertussis vaccine given May 9, 1911; whooping three weeks when treatment began; eight injections of forty million each were given. The patient was a delicate boy and was having paroxysms hourly day and night, with occasional vomiting. The patient began to improve after the first injection; vomiting ceased after the second injection. At the end of the treatment there was a little cough, but no whoop. Reported by Dr. John A. McCormick.

CASE 19.—John L., aged 2 months, brother of Patient 18, was given the first injection of pertussis vaccine May 9, 1911; whooping three weeks before treatment began; eight injections of forty million each were given. The case was moderate

in severity, and the patient was apparently much benefited by treatment. At the end of the treatment the cough occurred less frequently; the paroxysms were mild. Reported by Dr. John A. McCormick.

CASE 20.—Genevieve B., aged 15 months; treatment began May 8, 1911, after whooping had existed four weeks. The first injection of pertussis vaccine was on May 8; eight injections of forty million each were given. At the beginning of treatment the child had about sixteen paroxysms in twenty-four hours, ten during the day and six during the night. The paroxysms were very severe, with frequent vomiting and cyanosis; improvement began after the third injection; distinct improvement was noticed after the fifth injection. At the end of treatment the child was still coughing, but only an occasional whoop. Reported by Dr. John A. McCormick.

CASE 21.—John B., aged 3 years, brother of Patient 20; first injection of pertussis vaccine May 8, 1911; whooping three weeks when treatment began; eight injections of forty million each were given. The case was of more than ordinary severity. The paroxysms occurred about once an hour day and night, with cyanosis and vomiting. The cyanosis and vomiting disappeared after the fourth injection. After the fifth injection, the mother thought the child was well enough to stop the treatment; eight injections, however, were given. At the end of the treatment, the child was almost entirely well, with practically no cough and no whoop. Reported by Dr. John A. McCormick.

CASE 22.—Edward S., aged three years, treatment began May 8, 1911. Hemorrhage into the conjunctiva occurred as the result of the severity of the paroxysms. No improvement was noticed until after the fourth injection. Vomiting ceased after the sixth injection. The patient received nine injections of forty million each. At the end of the treatment the boy was very much improved, although he still coughed and whooped occasionally. Reported by Dr. John A. McCormick.

CASE 23.—Emma M., aged 9 months; first injection of pertussis vaccine May 6, 1911. Whooping commenced one week before treatment began. Seven injections of forty million each were given. Cyanosis and vomiting were frequent at the beginning of treatment. Paroxysms occurred at least every hour during the day and five or six times during the night. At the end of the treatment the paroxysms were few in number and less severe, but the child was still coughing and whooping occasionally. Reported by Dr. Scott Lau.

CASE 24.—William B., aged 5 years; first injection of pertussis vaccine May 8, 1911; whooping eleven days before treatment began; eight injections of forty million each were given. The case was one of moderate severity. At the end of treatment the paroxysms of coughing were much fewer in number and less severe, although the boy still coughed and whooped occasionally. He was distinctly benefited by the treatment. Reported by Dr. Scott Lau.

These reports do not represent the true worth of the remedy, as I believe better results would surely have been obtained had larger doses of the vaccine been employed; 40 million may be, and probably is, a sufficient dose for a mild case in an infant or young child. One hundred million would be a much more suitable dose for a severe case, regardless of the age of the patient.

Of the twenty-four reported cases, seven were apparently not benefited by the treatment, the disease evidently pursuing its usual course in about 29 per cent. Seventeen patients, or about 71 per cent., were apparently benefited by the treatment. I believe the dose could, and should, be increased beyond 40 million, especially for severe cases; 60, 80 or 100 million will probably be a more efficient dose. The results obtained in these twenty-four cases warrants, in my opinion, a more extensive trial of the vaccine.

THE RADICAL REMOVAL OF THE TONSILS AND ADENOIDS

CHARLES G. KERLEY, M.D.

Professor of Diseases of Children, New York Polyclinic Medical School and Hospital; Assistant Attending Physician, Babies' Hospital of the City of New York; Attending Physician, New York Nursery and Child's Hospital

NEW YORK

During the past ten years I have performed the operation for the removal of tonsils and adenoids 371 times in private practice. All but one were my own patients. A much larger number have been operated in hospital and out-patient work. These are not included in this article for the reason that many could not be followed so as to know the ultimate results.

Until eighteen months ago the method of procedure was to remove as much of the tonsil as possible by firm pressure with the tonsillotome and counter pressure by an assistant, but without any attempt at dissection or complete removal of the tonsil. This resulted in the removal of perhaps two-thirds or seven-eighths of the tonsil, leaving the capsule and some tonsillar tissue. The great majority of my cases so operated on were benefited permanently, that is, benefited somewhat. In others the benefit was very temporary, the tonsil soon assuming the former size, the new growth showing connective-tissue changes and adhesions to the pillars, which made the condition worse than it was before the operation. Even in the cases in which a regrowth of the tonsil did not occur we had the same tendency to tonsillitis and the tonsil as a portal of entry for bacteria continued to be an active agent. Further, second and third operations have been necessary under this procedure. I have performed the second operation after different operators as well as in my own cases.

It is not particularly flattering to be told that the tonsils which *you did not remove* have returned, with emphasis on the *did not,* and all men who have operated much by the above method have had this experience.

I had for some time appreciated the desirability of a complete removal of the tonsil, but had been unfavorably impressed with the method employed. The elaborate dissection with many instruments, the deep and prolonged anesthesia, the large loss of blood, the resulting prostration and the slow convalescence made an operation the severity of which was

not warranted in the results attained. It was accordingly with a great deal of interest that I learned that a method of *finger enucleation* was being carried on by Dr. Frank S. Mathews of New York City. Later, December, 1908, Dr. Mathews described this operation in the *Annals of Surgery*. The method advocated occasioned a good deal of adverse comment, and I did not begin to practice it generally until eighteen months ago.

Forty-eight hours before the operation 10 grains of lactate of calcium is given three times daily, the last 10 grains being given after 8 ounces of chicken broth on the morning of the operation. I am convinced that the lactate of calcium lessens the amount of hemorrhage. The method of procedure is as follows, and differs but little from that of Dr. Mathews. Ether or gas-ether anesthesia is used. The anesthetic is given to the point of abolishment of the corneal reflexes. The child is gagged sufficiently to allow the entrance of and to give the index finger free play. Our object is to perform a tonsillectomy to strip the tonsil from its bed. For the right tonsil I pass my right index finger into the mouth, and with moderate pressure and finger point dissection pass the finger into the superior fossa at the junction of the anterior and posterior pillar. I thus go in above the tonsil, work down behind the capsule, pull the tonsil downward and with pressure exerted first anteriorly and then posteriorly separate it from its attachments until it hangs by a pedicle formed by the mucosa and blood-vessels. Over this as small a tonsillotome as will engage the tonsil is slipped. The anesthetist makes firm pressure from without and the operator with firm pressure on the tonsillotome within cuts the pedicle. No tonsil tissue is cut. The blood-vessels in the pedicle contract readily without the interference of firm connective tissue.

Mathews places the gag to the opposite side from that which is to be operated. I do not find this necessary except in very young children or in those with small mouths.

For the left tonsil exactly a similar procedure is carried out, excepting that the left finger is used. I have had but little difficulty in removing the entire tonsil by this method.

The 371 cases represent every type of tonsil. The deeply imbedded strip out as readily as those more superficially placed. The duration of the entire operation, including the anesthesia, rarely requires more than six minutes, and this includes the removal of the adenoids which may be present. In order to do thorough and rapid work the anesthetist must be not only expert, but accustomed to work with the operator.

Dr. R. S. Haynes, who has assisted me in a great many of these operations, has timed our visit from the time we entered the house until we left it, and found it oftentimes not more than twenty minutes. When the patient is removed from the table he is sufficiently out of the anesthesia to cry vigorously. He is given nothing but broths and gruels for the day. An enema at 5 p. m. is given. The following day he sits up in bed and plays. The next day he is up and about and the next day out of doors. Neither ice-cream nor milk is given the day of the operation. I have experienced no little trouble with children who were given milk or ice-cream within a few hours after the operation. It is very apt to result in indigestion and high temperature, which alarms the family, who are inclined to attribute it to infection or something else very alarming.

It is claimed by the opponents of this finger method that complications follow the operation and that there are end results which are distinctly harmful. I have had one case of postoperative adenitis which responded promptly to local cold. The child had a temperature of 102 F. to 104 F. for three days. I have also had one case in which adhesions were formed by the pillars growing together. I have had no excessive hemorrhage at the time and no postoperative hemorrhage. This, I believe, is due to the fact, as mentioned before, the tonsil tissue is not cut, and the vessels in the pedicle readily contract. The rôle played by the lactate of calcium is an uncertain one, but those who have used it, together with myself, believe that the hemorrhage is lessened thereby.

During the past eighteen months I have performed 137 enucleations by the above method. Rarely has it been necessary to use anything other than the finger. In three or four instances a pillar separator and blunt curved scissors have been necessary. The only instruments required have been the gag, the tonsillotome and an adenoid curet.

Adenoids.—The removal of the adenoids is very simple and requires but a few seconds. I use a modified Gottstein curet, which is built at an angle of about 45 degrees. This curet is very sharp. I have long since discarded the forceps as being unnecessary. Two or three sweeps of the curet and all the adenoid tissue, hard and soft, is removed.

Adhesions.—From six weeks to three months after the operation the nasopharyngeal vault is examined for adhesions. The adhesions are usually attached anteriorly to the posterior surface of the inferior turbinates and oftentimes extending in a fan-shaped form to the posterior and lateral wall. My attention was first attracted to the presence of these adhesions by mothers who brought their children for treatment and who

would state, in getting their history, that the adenoids had been removed and the child was relieved for a few months when the obstruction became as marked as before. The operator was naturally blamed for not completely removing the adenoid tissue.

Examination of the vaults in these cases disclosed the adhesions. The adhesions are usually readily removed with the finger. I have seen three cases, however, in which this could not be done on account of the firmness of the adhesions. One was recently operated by a New York laryngologist for relief of the condition. Besides limiting the usual breathing space, these adhesions may be the cause of cough, which may be very teasing and troublesome.

A girl of 9 years came to me because of a persistent cough, which had continued during the winter and which could not be relieved. She had been operated for adenoids four years before. I found fairly firm adhesions, which were reduced with the finger. The cough stopped at once. The mother then brought me two other children on whom the operations had been unsatisfactory, both showing adhesions.

The existence of these adhesions is denied by many operators. I have found them after operations performed by men who said they did not know of them. Every man will find them in many of his cases if he will introduce his finger in the vault and search for them.

BENEFITS OF THE OPERATION OF REMOVAL OF THE TONSILS AND ADENOIDS

The usual advantages claimed, those relating to mouth breathing, facial deformities, etc., are sufficiently well known to be omitted before this audience. I would call your attention, however, to certain benefits that are not perhaps generally appreciated.

In Delicate Children.—In my office work I have occasion to treat every year a large number of children who come because of defective growth, who are suffering from secondary anemia, or who are in some way delicate. I have found these children remarkably improved by the removal of diseased tonsils and adenoids which are very apt to be present.

Scarlet Fever.—I have been surprised to note the ease with which children ill with scarlet fever will pass through an attack when they had normally resistant throats.

Adenitis.—Adenitis, tuberculous and otherwise, is a very unusual occurrence in a child who has had his adenoids and tonsils properly removed.

Among the large number of cases operated on I have yet to hear a regret expressed by the parents because the operation had been performed. I have myself had occasion repeatedly to regret that a complete enucleation had not been performed in my earlier cases.

Conclusions.—The finger enucleation method is best because of its rapidity. The child is kept under the anesthetic but a very short time.

Completeness.—The entire tonsil is removed with little or no cutting of the tonsil.

Absence of hemorrhage for reasons already given.

Few instruments required.

Short convalescence.

DISCUSSION

DR. ROTCH: I think we should remember in considering the subject of tonsils in children that the process of development must be taken into account. Normally adenoid tissue occurs up to a certain age, 4 to 6 years, and then tends to diminish up to about the fifteenth year. This accounts for the recurrences when early removal is practiced. I do not know whether this radical enucleation puts an end to the normal growth, but if one operates later than the fourth to sixth year there is certainly not so great a tendency to recurrence.

Then again we notice that it is not always the enlarged tonsils that produce the ill effects on the child, but that absorption from a small amount of diseased tonsil affects the health of the individual. Tonsils, therefore, which are not much enlarged must often be removed for this reason. These children suffer from debility and other treatment has no effect until this small amount of diseased tonsillar tissue has been removed.

DR. LA FÉTRA: It happens that when Dr. Mathews was first working out his technic of finger dissection I had a talk with him and he showed me some of the tonsils he had removed by this method. Ever since that it has appealed to me as the most satisfactory procedure. All of us have heretofore had recurrences; so that now, wherever possible, I have adopted this method of complete removal, and the results are most satisfactory. One doesn't have a fear that there will be a recurrence. Another advantage is that we do not see the severe attacks of sore throat such as occurred often after the tonsils were simply sliced off. There may sometimes be a little pharyngitis, but it is very slight.

As to the technic, there are certain cases in which the separation of the tonsillar pillars from the tonsil, if it has been the seat of repeated attacks of inflammation, is very difficult and the use of a separator will be found necessary in more cases, I think, than Dr. Kerley's paper would indicate. If one operates on a child of 6 or 7 years who has had frequent attacks, the capsule will be found adherent, and if one tries to enucleate the tonsil with the finger alone the tonsil will shell out from the capsule and there will be the same kind of bleeding as occurs where the tonsil is sliced off. There is also some danger of tearing the tonsillar pillars, anterior or posterior.

As to the adenoid curet, we should remember that it is not a curet in the ordinary sense of the term. As Dr. Kerley indicated, he has the blade of the curet very sharp, and I have found that by keeping in mind the idea that I am using a knife and making a lateral motion with the curet I can cut rapidly across

the base of the adenoid so that it is removed in one piece, with one cut, and that is more satisfactory than making two or three sweeps with it, as in using a curet.

DR. KOPLIK: I do not operate myself on tonsils or adenoids, and so will not attempt to discuss that part of the paper. In the early part of the paper Dr. Kerley refers to recurrences; I do not think anything is more discouraging than the cases that have been around to a number of the leading operators and have been operated on two or three times for adenoids and then still have symptoms of obstruction in the nose and postpharnygeal space. It is an obstruction not due entirely to adenoids, but to a thickening of the whole mucous membrane and adenoid tissue under the mucous membrane. Repeated operations really harm this particular class of children. There is no doubt that in the majority of cases one operation not only relieves the child and places it in a better condition, but that is all that is necessary. The whole subject, however, is not as simple as it has been made to appear here this morning. Some of the cases require a great deal of consideration as to when the operation should be done and as to whether any benefit may be expected from operative procedure.

There are also other forms of tonsils which practitioners and specialists seem anxious to take out; the small tonsils, in young babies. The parents come and ask advice as to whether or not an operation should be done. I have seen several of these cases operated on wherein it seemed to me that the condition of the child was worse after the operation than before. This does not refer, of course, to those cases spoken of by Dr. Rotch wherein small diseased tonsils are evidently causing trouble. The tendency, I think, to-day is not to be so anxious to remove the entire tonsil. The feeling is that the tonsils have been placed there for some purpose and a future study may show what that is. With laryngologists, who after all are the ones who have given the most thought to this subject, there is a tendency to leave a little tonsillar tissue behind.

As to the danger of the operation, I have seen two cases of endocarditis following enucleation and in the hospital others have seen similar cases. These conditions of endocarditis are very disquieting because they persist for quite a long while. I recall that one case was very much so. I have seen severe diphtheria occur on the seat of the tonsillar fossa after complete enucleation of the tonsils.

DR. FREEMAN: I think this matter of total extirpation of the tonsils is of great importance. If we look on the tonsils as part of the normal mechanism for protecting the organism from infection, it is a question if they should be entirely removed. If they should not be, then one might expect after their removal to see an infection of the cervical lymph nodes in place of the tonsils. Dr. Kerley has mentioned such a case, and in the first case I had in which the tonsils were entirely removed a month later there was a severe infection of the cervical lymph nodes. It is questionable if it is not better to leave some of this tissue.

DR. HAYNES: It seems to me that of all complete methods of removal of the tonsils, the finger enucleation is the simplest and is accompanied by the least hemorrhage and after-prostration. It has been my experience that the cases wherein there has been much hemorrhage have been those in which the dissection has been done with sharp instruments.

Dr. Kerley has said that his operation takes about six minutes. I have timed him and I think that is a conservative estimate; but to do an enucleation in this time requires an operator who can work with primary anesthesia, for this six minutes includes the giving of the anesthetic.

Calcium lactate certainly lessens the amount of bleeding at the time of operation.

The curet seems to me the only instrument needed in the removal of adenoids except in certain instances wherein the tissue is placed so far forward that it comes into apposition with the vomer and the curet cannot engage its anterior edge. Then the forceps must be used. It is of help in getting out the adenoid in one piece to feel with the forefinger of the left hand through the soft palate and ascertain the exact position of the curet, and whether or not the adenoid mass is prolapsed through the ring. If it is, a single sweep will nearly always clear the vault.

DR. KNOX: I should like to ask Dr. Kerley as to the age of his patients that he operates on and what he considers are the indications for removal of adenoids in young babies? Also whether the results have been as good as in the older children.

DR. CHAPIN: There is one point I would like to bring out, that of the condition of the bony structure above the pharynx. A certain number of these cases have a Gothic arch instead of a round one, and in my experience children of that sort do not get such relief from the adenoid operation as do those who have a wider arch. In some cases symptoms that are assumed to be due to adenoids are really due to this underlying condition of faulty development. This used to be referred to as a strumous condition. We must remember that some of the symptoms attributed to adenoids may really be due to this underlying developmental vice.

DR. JACOBI: I notice that this operation of tonsillar enucleation is no longer a monoply. A few years ago it was so considered. Books have been written to show that it was a very difficult operation and that the patients should all be sent to the author for operation. About five years ago the prevention of tuberculosis was considered possible by the removal of tonsils. One man stated that tuberculosis could be prevented by enucleating the tonsils, but that it must be done completely, and that he could do it. I have been told in New York that it was a very difficult operation. I now learn to my satisfaction that the operation is not so very difficult any more; that it is very easily performed.

I do not believe that it should be done so frequently as some gentlemen seem to think, for the very simple reason that it is not a matter of indifference whether the capsule is removed or not. The capsule is a protection to the blood and lymph circulation. I believe that more and more we shall learn that infection through the protecting capsule is rather difficult. We shall learn that the infection of rheumatism and scarlet fever through the capsule is not so frequent but that it takes place through the soft lymph-nodes of the Waldeyer ring.

Another point: I have seen a great many operations and the results, and have done the operations myself. I find that the operation is easy, particularly that on the adenoids, and that is often about the only concern of the operator. He packs up and goes home. That is not, however, enough for the child. The child's nares should be attended to afterward and before. If the nares were properly attended to more frequently than is done, a great many of these operations would be unnecessary. A clean nose does not grow adenoids as an unclean one does. A great many of our catarrhs, acute and chronic, would be better if the nares were attended to by proper irrigation, not, however, injections; injections are dangerous to the ears; irrigations never are. The liquid never runs into the ear unless it is snuffed up. It should be an irrigation with a small quantity of liquid at a time from a cup, not through an atomizer,

and not snuffed up. If the nares were kept clean—I repeat this again, particularly for the benefit of those who operate so much—there would be a great deal less necessity for these operations. And after the operation the nose should be attended to just as before, carefully, not only for a few days or weeks, but for perhaps years. It is very easy; children get used to it and it can be done more readily than washing out the ears. Recurrences of this condition would be avoided in this way by irrigating the nares with a lukewarm normal salt solution.

DR. KERLEY: The point made by Dr. Haynes is an excellent one, that of locating the adenoid with the finger in the postnasal space before using the curet. I always do this. The size and shape of the vault is of importance, as Dr. Chapin has pointed out. It is because of the difference in the size and shape of the pharyngeal vault that a very small adenoid in a very small throat may cause a lot of trouble and may require removal where in a wider vault it would not. As to the age of the patient, I try to avoid operating on children under 1 year as I think the younger the child the less we should be inclined to operate, especially so far as the tonsils are concerned. I do not recollect operating on a patient under 18 months of age. However, I think adenoids should be removed regardless of the age of the child, if sufficient to produce obstruction. One of my patients was 8 months old. I did not mention diphtheria because I have not seen a case following enucleation.

Dr. Koplik has spoken of endocarditis occurring after the tonsils have been enucleated—two cases. Dr. Koplik has seen a great many cases occurring wherein tonsillectomy had not been done. How does he know that the tonsillectomy had anything to do with the condition? The laryngologist is perhaps not a safe man to follow as far as results are concerned. He does his operation and then the patient is returned to the pediatrist or general practitioner, who has to take care of it, and he has an opportunity to check up and see the results of the work.

Dr. Chapin has spoken of the function of the tonsil; we do not know anything as to its function, but I do know that the tonsils I take out have no function because they are riddled with holes and constructed of connective tissue, and if there is any function in this connective tissue and crypts filled with bacteria, then I would like to have some one show me what it is. What function can there be in a diseased tonsil? Of course, we are not taking out healthy tonsils. Adenoids do return, but that is no reason why they should not be removed a second or a third time if necessary. You may take them out in a child 4 years old and find that he has another crop at 6, but it is simple enough to remove them again. I have had to operate on one child three times. He outgrew the tendency to grow this lymphoid tissue and the third operation was sufficient. He would grow a vault full of adenoids in the course of a year and the parents would again have them removed. If you wait, the patient develops a tubal catarrh and all the facial malformations that this condition of obstructed nasal breathing may cause.

THE OCCURRENCE OF INFANTILE PARALYSIS IN THE UNITED STATES AND CANADA IN 1910

ROBERT W. LOVETT, M.D.
BOSTON

The great prevalence of infantile paralysis in the United States in 1910 and its rapid increase in the last two or three years in this country, are matters which demand our serious consideration, and in the following paper will be presented the data obtainable on the subject, preceded by a brief résumé of the history of the disease in this country insofar as it bears on the present situation.

That infantile paralysis is not a new disease is a matter of common information, and it is of interest to note that the first probable allusion to it to be found in literature occurs in the book of Samuel, fourth chapter and fourth verse. It is as follows:

> "And Jonathan, Saul's son, had a son that was lame in his feet. He was five years old when the tidings came of Saul and Jonathan out of Jezreel, and his nurse took him up and it came to pass as she made haste to flee that he fell and became lame. And his name was Mephibosheth."

This short clinical history, although suggestive, is hardly convincing, but it is quite as likely to have been a case of infantile paralysis as are some of the cases reported as such in the year 1910.

The disease is first recorded as occurring in America in epidemic form in 1841 by Colmer,[1] as follows:

> "While on a visit to this parish, West Feliciana, Louisiana, in the fall of 1841, my attention was called to a child, 1 year old, slowly recovering from a hemiplegia. The parents, who were people of intelligence and unquestioned veracity, stated that either eight or ten cases of either hemiplegia or paraplegia had occurred during the preceding three or four months within a few miles of their home. Some of these recovered completely, others were improving. The little sufferers were all under 2 years of age and the cause seemed to be the same in all, viz., teething."

The account of this epidemic has, however, been questioned on the ground that it was only hearsay evidence and not substantiated, and the

1. Am. Jour. Med. Sc., 1845, v, 248.

first authentic description of an epidemic of thirteen cases is credited to Bergenholz, a Swede, in 1881.

That infantile paralysis has existed in the United States for an indefinite time is perfectly familiar to us from the fact that we all know of adults affected whose history would reach back fifty years.

In 1875, Sinkler[2] reported that in the preceding four years he had seen eighty-six cases at the Infirmary for Nervous Diseases in Philadelphia.

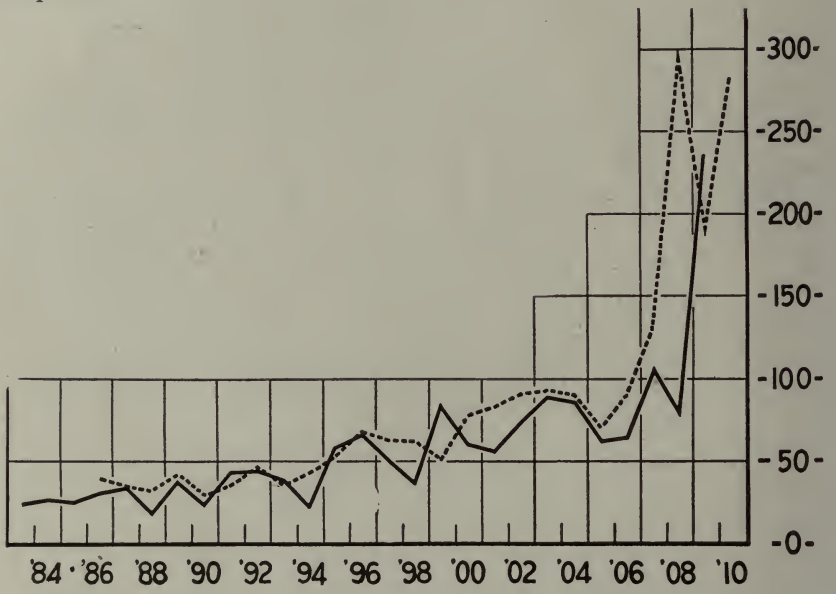


Chart 1.—Number of new patients with infantile paralysis treated at Children's Hospital, Boston, indicated by the solid black line; those treated at the New York Orthopedic Dispensary and Hospital by the dotted line; both by years.

The best evidence that I can find of the existence of infantile paralysis in our midst in any considerable degree for the last twenty-five years is derived from a study of the records of two hospitals, one in Boston and one in New York, which also contribute the best evidence that I have seen of the sudden increase of the disease in our midst in the last few years. The first named of these hospitals draws from a large area and the clientele of both in the last twenty-five years has been more or less constant.

2. Sinkler: Boston Med. and Surg. Jour., Nov. 23, 1893.

The accompanying chart (Chart 1) is constructed in part from the records of the orthopedic out-patient department of the Children's Hospital, Boston, and shows the number of new patients with infantile paralysis applying for treatment since 1883 in that department. The figures show that in 1883 we treated twenty-two patients, and that the number of cases with unimportant fluctuations rose steadily for twenty-five years, until 1909, when Boston was an epidemic center, when it rose suddenly to 235 cases.

The second institution analyzed on the chart is the New York Orthopedic Hospital and Dispensary, the figures of which were kindly furnished to me by Dr. Russell A. Hibbs, and which show in general the same facts. There were thirty-nine new cases in 1886, rising gradually to 1907, when a marked increase occurred. It will be noted that the New York increase began two years before that in Boston.

The first outbreak in the United States of the disease in any considerable degree was in 1894, when Caverly[3] of Rutland described an epidemic of 132 cases in the Otto Creek Valley, Vermont. In this epidemic Caverly attended to abortive cases, not under that name but as cases presenting the clinical symptoms without the paralysis.

In the same year was reported by Brackett[4] a group of ten cases in North Adams, Massachusetts. Both Rutland and North Adams are in railroad communication with Boston, and it is interesting to note that Putnam[5] in November of the previous year, 1893, had called attention to the increased prevalence of the disease in Boston in the preceding summer, the patients coming from different parts of the suburbs of Boston.

In the following eleven years, that is, from 1894 up to 1904, there were reported in the United States nine small epidemics (Chart 2), the second largest again in Massachusetts, consisting of thirty-eight cases,[6] and the largest, fifty-five cases,[7] in California, about San Francisco. The total epidemic cases reported in these eleven years, i. e., from 1894 to 1904, inclusive, in the United States were 157, or an average of about fifteen a year.

3. Jour. Am. Med. Assn., 1896, xxvi, 1.
4. Brackett: Tr. Am. Orthop. Assn., xi, 132.
5. Putnam: Boston Med. and Surg. Jour., Nov. 23, 1893.
6. Painter: Boston Med. and Surg. Jour., cxlvii, 633.
7. Wood's Occidental Med. Jour., xvii, 77.

In 1905-6 no epidemics were reported.

In 1907 the most extensive epidemic ever known visited New York City and its surroundings and was estimated at 2,500 cases. In the same year were reported epidemics in Virginia (26 cases), Pennsylvania (100 cases), Massachusetts (234 cases), Michigan (20 cases), and Northern New York (29 cases); a total of about 2,900 cases.

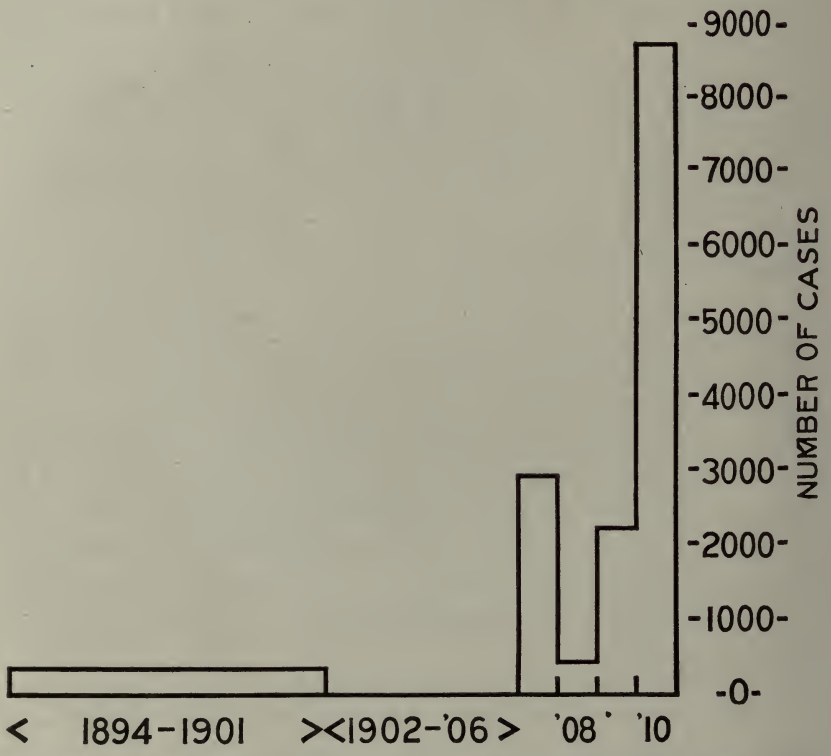


Chart 2.—Prevalence of infantile paralysis in the United States, 1894 to 1910.

In the year 1908 the disease was apparently quiescent, groups of cases being reported from Massachusetts (136), Michigan (30), Florida (16), Minnesota (60) and Wisconsin (60); a total of 302 cases.

In the year 1909 large epidemics occurred in Massachusetts, Minnesota, Kansas, Nebraska and Cuba, the total number of cases being 2,343.

When we come to the analysis of the figures for 1910 we must remember that they were brought out by a systematic and extended inquiry undertaken by the Massachusetts State Board of Health, and probably

had such an inquiry been possible in one of the earlier years a larger number of cases would have been discovered than now stand as reported in those years. Still, one cannot conceal the fact that in 1910 there apparently occurred a very much larger number of cases than before all over the United States, and that the extent and distribution of the disease in this country in 1910 was of a different character from that of any previous year.

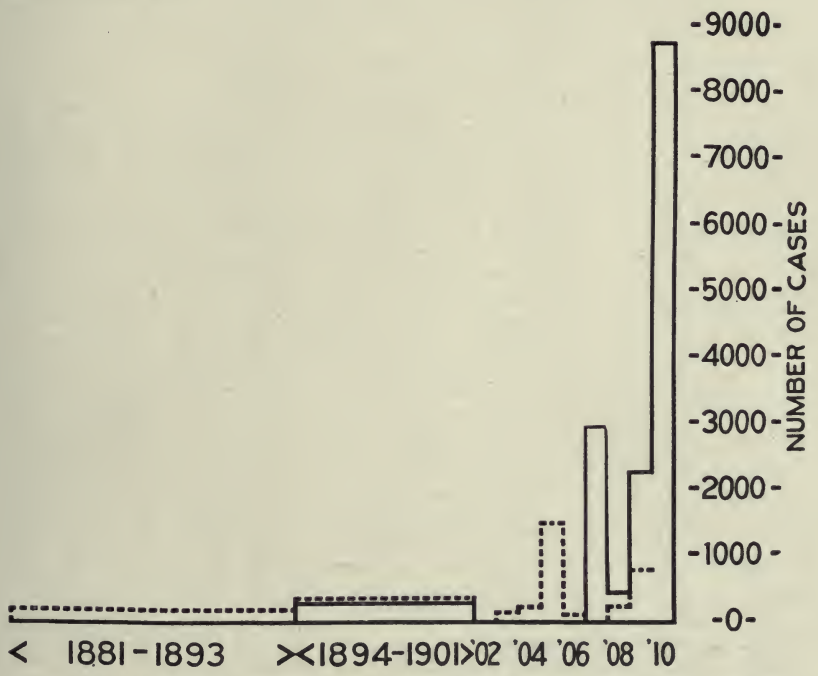


Chart 3.—Relative prevalence of infantile paralysis in the United States and Europe and Australia; the solid black line refers to the United States; the dotted line to the following countries: Italy, Sweden, Norway, Germany, Austria, France, England and Australia.

There were about 8,700 cases reported in the United States in 1910, and if we contrast that figure with the years prior to 1904 when the average yearly number was fifteen cases per year we may appreciate what an enormous increase has occurred.

To summarize for a moment our facts so far collected: The disease has unquestionably existed in this country for many years. In 1893 the first reported tendency to increase is said to have showed itself

in Boston, followed by the Vermont epidemic in 1894, and in the next eleven years by other small epidemics in various parts of the country. Then came a period of quiescence followed by a violent outbreak in New York in 1907, since which, on the whole the extension of the disease has been rapid and in all directions. We are evidently now facing conditions favorable to the spread of the disease which did not exist in former years, and conditions which do not exist in Europe now, and it is for the purpose of bringing out this very point that I have thus dwelt on the earlier history of the disease in this country.

In Europe, although there has been an undoubted tendency of the disease to spread since 1905, when the great Scandinavian epidemic occurred, five-sevenths of 8,000 cases reported from all over the world for the five years ending in 1909 occurred in this country. The relative prevalence of the disease on the two continents is shown in the chart (Chart 3) and needs no comment. The disease is a reportable one in Sweden, Norway, Germany and Austria, so that in these countries, in any event, epidemics are not likely to fail to be reported.

The data with regard to the disease in the United States in 1910 were collected as follows: Dr. M. W. Richardson, the secretary of the Massachusetts State Board of Health, sent out several hundred letters of inquiry to state boards of health, to officers of state medical societies and to prominent physicians in various parts of this country, its dependencies, and Canada. From their replies to those letters the data given in Table 1 have been compiled. In a few instances the figures have been taken from the Marine Hospital Service tables prepared by Frost, and such are marked (F). In certain instances where no reliable number of cases or no number at all was given in a state, and the number of deaths from infantile paralysis during 1910 was given, the number of deaths has been multiplied by ten, a conservative mortality per cent., and the number of probable cases thus estimated. In such cases the figures have been followed by the abbreviation (Est.).

Mortality per cents. have not been allowed any importance in this tabulation, as they are only of value or significance in instances in which an epidemic has been carefully enough studied to bring out the total number of cases occurring. For example, one state in which the disease is not reportable, reports thirty-five cases and thirty deaths, which probably does not mean that the mortality was enormously high in that state, but that the deaths were reported and the non-fatal cases were not.

Although somewhat lower than the figures in foreign countries, there is reason to believe that the Massachusetts figures of 8 per cent. are approximately correct for that state at least, although the mortality per cent. in the District of Columbia in 1910 was only about 3 per cent.[8]

TABLE 1.—DISTRIBUTION OF INFANTILE PARALYSIS IN THE UNITED STATES, 1910

Alabama*	Few	North Carolina	Few
Arizona	30 Est.	North Dakota*	150
Arkansas	No information	Ohio*	52 F.
California	100	Oklahoma*	20
Colorado	9 F.	Oregon*	112
Connecicut	168	Pennsylvania*	1000+
Delaware	8	South Carolina*	85 F.
District of Columbia.	500	Rhode Island	231 F
Florida	19	South Dakota*	86
Georgia	Few	Tennessee*	None known
Idaho*	96 F.	Texas	Few
Illinois	137 F.	Utah*	120 Est.
Indiana*	500 Est.	Vermont*	48
Iowa	651	Virginia*	350
Kansas*	198	Washington*	300
Kentucky	Few	West Virginia	Rare
Louisiana	50 Approx.	Wisconsin*	370 Est.
Maine*	Present	Wyoming*	Rare
Maryland	300 Est.		
Massachusetts*	845	Hawaii*	33
Michigan	43	Porto Rico	Absent
Minnesota*	1000	Alberta	11
Mississippi	Rare	Canal Zone	1 White
Missouri	174	Philippines	None
Montana	170 Est	Newfoundland	1
Nebraska*	50	Nova Scotia	Present
Nevada	9 (1909-10)	Ontario*	179
New Hampshire	210 Est.	Prince Edward Islands	None known
New Jersey*	70 (1909-10)	Quebec	Present
New Mexico	None known	British Columbia*	75
New York*	225	New Brunswick	Few

*Disease reportable by law. (In states not starred disease is not reportable by law.)

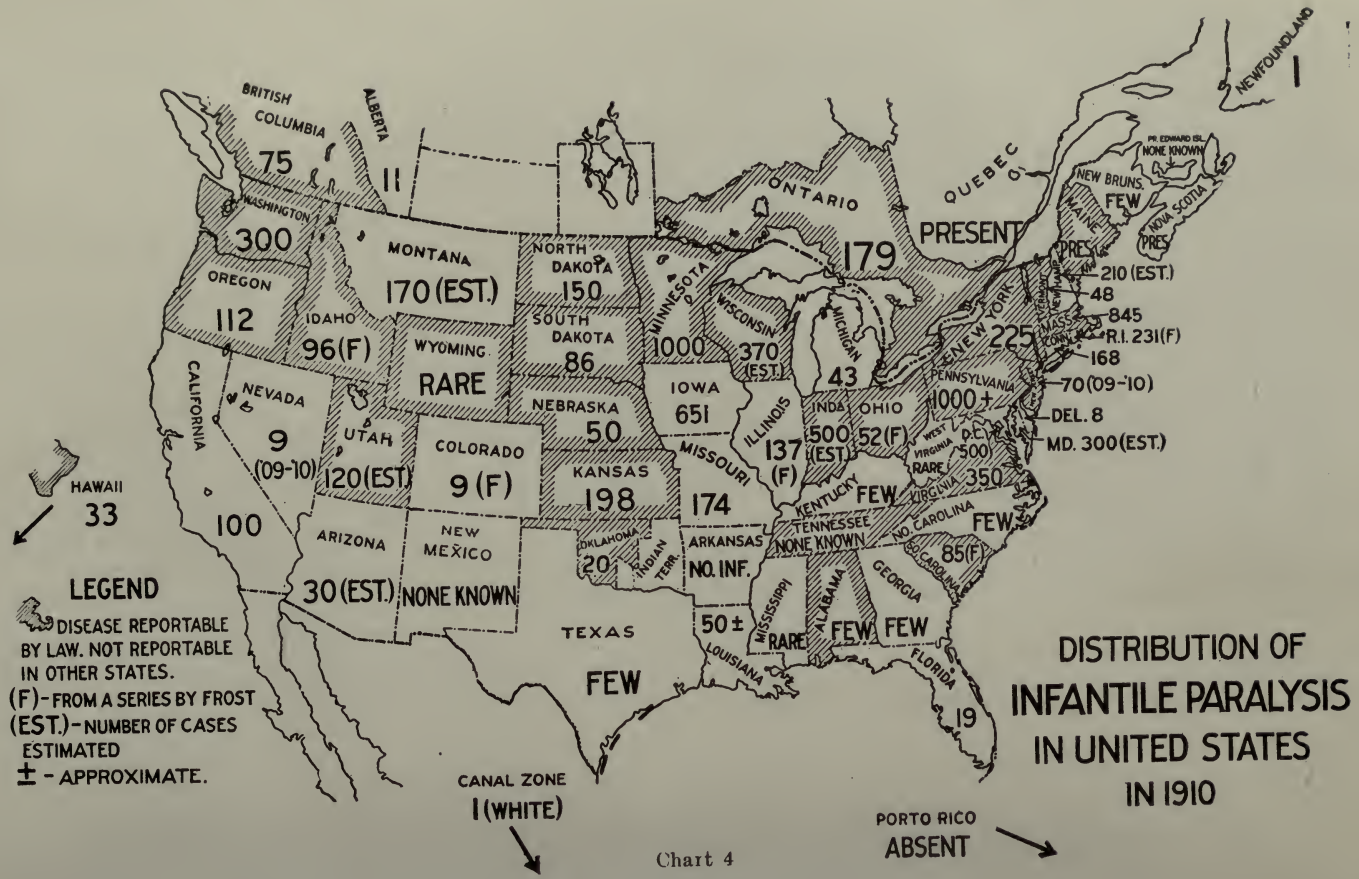
Est.—No of cases estimated.

F.—From series by Frost.

Approx.—Approximate.

The map of the United States (Chart 4), on which has been marked the number of cases in each state for 1910, shows a total of about 8,700 cases, not counting Canada or such dependencies as Hawaii, and making no account of states reporting "a few," etc. In practically all cases

8. Washington Med. Ann., May., 1911.



DISTRIBUTION OF INFANTILE PARALYSIS IN UNITED STATES IN 1910

Chart 4

not otherwise designated, the number of cases given is the number officially given out. Various terms have been used in the cases of states from which exact information was not obtainable, the term being chosen according to the information which was sent in.

The disease is now reportable by law in twenty-three states, which are shown shaded on the map, and various other states have the matter under consideration or may have legislated very recently.

A study of this map shows in the first place a wide-spread and general distribution of the disease with, in general, a focal occurrence and radiation from these foci. There is in general a scarcity of cases in the southeastern section of the country. In the New England states there occurred a group of cases, the largest number being in Massachusetts and Rhode Island. It is probable that the large number credited to Massachusetts is in a measure due to the careful investigation of the disease carried on there now for four years, as a result of which the medical profession is on the alert to report cases, so that the apparent prevalence there is probably exaggerated in comparison with other states.

An epidemic focus of considerable size existed in Pennsylvania, Maryland, North Carolina and Virginia, the latter state being the southern limit of any considerable extension in the East.

In the Middle West there was a large epidemic focus in Minnesota, Wisconsin and Iowa, some 2,000 cases being reported from these states, and in a circle around these three seriously infected states there existed in neighboring states from fifty to 200 cases per state, with over 500 cases in Indiana. An area of comparative immunity from north to south covered the Rocky Mountain region, but on the Pacific Coast there existed in Washington an epidemic center of 300 cases, with extension south to California and general involvement of the Southwestern states.

In Canada the disease appeared most extensively in the Province of Ontario, with 179 cases, with seventy-five in British Columbia and eleven in Alberta. New Brunswick reported a few cases, but no deaths, and there were cases in Quebec and Nova Scotia, with one in Newfoundland, but Prince Edward Island reported the disease as unknown there in 1910.

The disease is reportable by law in Ontario and British Columbia and not in the other provinces.

As to our Southern dependencies, there were no cases in Porto Rico or the Philippines; one in a white laborer in the Canal Zone, and an epidemic of thirty-three cases in Hawaii.

It is disquieting to note that in April of this year (1911) an epidemic of twenty or more cases occurred in Louisiana,[9] which was so threatening that the governor was appealed to for aid in suppressing the epidemic. In Massachusetts in the four years during which the disease has been under observation it has occurred earlier each year, reaching its height in September in 1907, August and September in 1908, in August in 1909 and in July in 1910. It will be of importance to note whether this is a mere coincidence or whether the disease is really tending to occur earlier as it spreads.

Such are the data that it has been possible to bring to light, but it is of course evident that the number of cases thus officially reported is a poor criterion by which to judge the total number that have occurred. In half of the states the disease is not reportable and it is naturally impossible to obtain any reliable information from these, and where it is reportable many cases are either unrecognized or unreported when recognized. The disease is so dreaded by the public that there will be a tendency to the suppression of information, especially in summer resorts.

In view of these facts, it may seem to this society worth while to take action to urge again on all state boards of health the importance of placing this disease on the list of those reportable by law. Several states in which the disease is not now reportable have the matter under consideration and the situation is too serious not to warrant every effort to place the disease where it may be studied and watched.

Several state boards have set on foot investigations as to the prevalence and distribution of the disease and have formulated blanks for distribution. But desirable as this is, we need more than this. The important questions that we want to have answered, the facts that will help us in finding out more about the disease, are not to be settled by the routine investigation of epidemics.

These are to be found in literature by the dozen, and anyone familiar with the subject can tell you in advance just what such an investigation will show. The disease will be found in scattered foci, with cases radiating from these foci. It will reach its height in the late summer; it will follow the lines of travel; it will affect mostly children in the first dentition; the mortality rate will be from 3 to 15 per cent. In October the epidemic will begin to die out. Data of this class exist in abun-

9. New Orleans Times Democrat, April 27, 1911.

dance and are useful only in giving us the distribution of the disease in a given locality.

What we do need is a careful house-to-house study, made, if possible, during the epidemic by competent medical men on salary, giving their whole time to the work. These men should examine most carefully the premises, the neighborhood, and every detail of the patient's life, environment and habits, his points of contact with other cases, with sick animals, the history of wounds and insect bites, his food, antecedent illnesses, etc.

The solution of the mystery of this disease may come from the laboratory or from the field work, or from both, but field work to be of any use must be intensive. The collection of routine data will not settle the question of etiology.

Such a plan as this means financial support, and in Massachusetts we have found the legislature ready to give us such support, and not only the legislature, but the public, a voluntary subscription of $5,000 from private sources having been placed at the disposal of an expert for the study of animal diseases akin to infantile paralysis. In addition to this the Massachusetts legislature of this year has appropriated $10,000 for the use of the State Board of Health in the coming year in the study of the disease. These facts show how a community feels where the disease has prevailed extensively.

Finally, it would be of value if some bureau or central committee for the interchange of information could be established with regard to the disease in America and the provinces. Such data as are presented above are only secured now by the expenditure of much effort and a considerable amount of work and money. If the disease is to increase in the near future at the same rate as in the last two years in America, it is important for the medical profession to have at its disposal every facility for obtaining information and every opportunity for study of the disease that is possible. On the one side we run the risk of alarming the community by the publication of such facts as these, but on the other hand, if we neglect to look at the situation as its exists, we run the risk of being charged later with having underestimated the seriousness of the present situation.

234 Marlboro Street.

THE CEREBRAL FORMS OF POLIOMYELITIS

HENRY KOPLIK, M.D.
NEW YORK

During the first epidemic of poliomyelitis and in the recurrent outbreaks in New York and vicinity there have occurred here and there a number of cases which have been of great interest because of their close simulation of certain cerebral conditions which I shall mention later. I refer to those cases of poliomyelitis which belong more particularly to the cerebral group of this affection. Polioencephalitis or encephalitis, as it is called, was first brought into closer relationship with poliomyelitis by Medin. In the large Swedish epidemic of 1905 there were many of these cases, and Medin in his early writings insisted on the general identity of this set of cases with poliomyelitis as it was then known. His assumptions were at first disputed by men of no less genius than Henoch, who thought that Medin in describing the cerebral forms of poliomyelitis as identical with the spinal forms in etiology and pathology had rather committed an error of clinical observation and mistaken his cases for something of another character. How certain and true the original observations of Medin have been time has shown, and Harbitz and Scheele have proven beyond question that the infectious agent producing epidemic poliomyelitis may extend to any part of the cerebrospinal system, and may affect both the gray and white matter of the brain and cord. Moreover, there is in all cases of poliomyelitis a real meningitis; that is, the processes of infection expend themselves on the membranes of the brain and cord. There is an inflammation and infiltration of these structures, and from the vessels of the pia the toxic or infectious agent enters the tissues of the brain and cord, there effecting changes of greater or lesser severity. Thus the consequent symptoms will differ in sets of cases according to the localization of the inflammatory processes at play.

The cases to which I especially desire to call attention are those in which the structures of the brain, medulla and pons are affected, leaving the cord for the most part unaffected permanently. These cases have been previously described by various writers as encephalitis or polioencephalitis superior or inferior of Wernicke or of poliomyeloencephalitis of Strümpel. We may group all these descriptive clinical

pictures under the entity of polioencephalitis. This would also include the pontine forms of encephalitis of Oppenheim. The general picture of polioencephalitis is cerebral, the symptoms are cerebral symptoms with, in certain cases, added palsies. Thus if the nuclei of the oculomotor nerves are affected we have with the cerebral symptoms an ophthalmoplegia of greater or lesser extent, identical with that which Wernicke describes as polioencephalitis superior. If the nuclei of the facial nerves are affected and the gray matter in the floor of the fourth ventricle, the cerebral symptoms are supplemented by facial palsies, and thus there is produced the picture described by Wernicke as polioencephalitis inferior. If the process extend still further down it may involve the nuclear masses of the hypoglossus and more vital nuclei, and then symptoms of paralysis identical with acute bulbar paralysis are produced. Certain it is that the forms of polioencephalitis will merge into one another. Thus, cases occur in which there are isolated palsies, such as those of the muscles, of one or other of the eyes; and then cases occur in which eye and facial nuclei (muscles) are involved, and others in which all these are affected and bulbar symptoms occur. The last group rather number the fatal cases, though I have seen a number of bulbar cases in which recovery occurred.

The cases which are limited in their extent of involvement of the ocular and facial nuclei, and which are accompanied by cerebral symptoms, are those which to me have been of greatest interest, because in such cases of polioencephalitis I have had the greatest difficulty, in the face of the cerebral symptoms, accompanied, as they were after a while, with nuclear palsies, to differentiate them from forms of meningitis either of the acute suppurative (meningococcic) variety, or the tuberculous forms of the disease. In fact, in some cases the clinical similarity of forms of polioencephalitis with forms of meningitis is so close that it is only by careful observation that we can differentiate the two, and then only with a possibility of some doubt. In order to facilitate clinical study of polioencephalitis it will be best to first draft in outline the general history of these cases.

A child in previously good health, without any marked prodromal symptoms, develops fever which may be quite high or may be moderate in degree. There may be complaint of some headache, there may be vomiting. Such a child will continue for twenty-four hours to be up and about, and after the initial period it is noted that the fever continues as does also the headache, and after a time the patient is too sick

to be about, complains of a tired feeling and goes to bed. It is then noted that the sopor deepens, and then the temperature may subside to the normal or continue a little above the normal. In some cases from this time on the history is that the patient is at times delirious, irrational, complains of headache, and resents being disturbed. There is extreme hyperesthesia. Some patients complain of pain in the nape of the neck; there is marked rigidity with the Kernig sign in the lower extremities, and signs of a mild hydrocephalus (Macewen). Such patients may have a maudlin delirium, lie crouched in bed and refuse to take food. Close examination may discover isolated ocular palsy in some cases, and this is the only objective palsy present. In other cases with palsy of some of the ocular muscles there is slight facial palsy of one or the other side, and in still other cases these palsies may be combined with a very mild weakness of one or the other upper extremity. After a week or two, the patient gradually becomes more rational, the sensorium is brighter and he begins to recognize objects and talk rationally. If during the illness the patient is caused to stand, there is noticed a very marked ataxia and vertigo, with Romberg's symptom. As convalescence is established, the ataxia is the last symptom to improve. The hydrocephalus may persist, the compromised mental capacities may not return to the absolute normal as soon as one would expect. The temperature has during the illness, directly following the period of invasion, been normal, or, in exceptional cases, there may have been a rise of 2 or 3 degrees, with a fall to the normal daily for a week or more. As the patients convalesce they are able to sit up, this not having been hitherto possible. Speech is more distinct, due to the recession of the ataxia.

This is a sketch of the common picture. When recovery is established there may remain a strabismus, or a very mild form of ataxia in the gait, an uncertainty as it were. In one or two of my cases I have seen optic neuritis, such as choked disk, in the course of the disease, and this also may retrograde, the eyesight being entirely restored. In other cases, the eyesight which has failed during the illness may progress to absolute blindness, and this in turn may slightly improve, as in one of my cases, so that after a lapse of months the eyesight may have improved from absolute blindness to the ability to distinguish gross, large objects. In another group I have seen a complete unilateral ophthalmoplegia with dilatation of the pupil of the affected eye.

I have related enough of the symptomatology of this form of encephalitis or polioencephalitis to show how close the similarity to a cerebrospinal meningitis may be, the sudden onset, the high fever, the rigidity of the neck, the headache, the Kernig, all run close to the symptom-complex of a meningitis, and yet close study will show some differences. There is in polioencephalitis a short preliminary period in which the patient, having had a high fever, continues to be about. There is also an increasing sopor which extends over days; this is quite unlike the onset of a cerebrospinal meningitis. In these two points we can sometimes differentiate between the two diseases. Here, however, the dissimilarity ceases. In a recent outbreak of polioencephalitis in Staten Island these two points stood out quite sharply on the clinical canvas, namely, the period of a day or so of high fever in which the patients did not quite take to bed, and then the period of fever and increasing sopor with the addition of all the symptoms of true meningitis.

Another set of cases of polioencephalitis are still more perplexing, inasmuch as they closely simulate another type of meningitis, the tuberculous form. A patient having been in previous good health will develop fever with some vomiting; the fever may be low, 102 or 103 F., or high, 104 to 105 F. The fever continues for a day or more and then sopor sets in, the temperature drops to the normal, the patient becomes completely unconscious. With this unconsciousness there is marked hydrocephalus, facial palsy, ocular palsy, such as strabismus, with loss of reflex at the knee, no Kernig, and a Babinski reflex. There may be a *tâche cérébrale*. After five or seven days of illness, the picture is the exact counterpart of a tuberculous case. The patient lies absolutely flaccid; there may be but very mild rigidity of the neck, there is Cheyne-Stokes respiration, and absence of reaction to mechanical stimuli in the presence of a normal or slightly raised temperature. After a few days the patient may succumb, but in many cases may come out of the coma and regain consciousness and power in the extremities. Such cases I have seen.

In another form the patient may have had a very short period of fever, which may have come on suddenly. Then after a few days the temperature falls to the normal, but the patient is noted to be stupid, and to act as if in a trance; there is mild hydrocephalus, but the sopor is the principal symptom. A bright child is noticed to act stupidly; begs to be left alone. There is hyperesthesia. All of these are present in face

of a normal temperature. Gradually the patient after two or three weeks becomes brighter, takes an interest in surroundings, and the ataxia, which in some cases amounts to absolute inability to walk, in others to staggering gait with vertigo, gradually improves. The similarity of these cases to tuberculous meningitis is exceedingly close. There is one very salient point of difference. In cases of polioencephalitis the onset is sudden. It is especially noticeable that the children have previously been in excellent health, when they are attacked by the disease within twenty-four or forty-eight hours at the most. In this respect the two maladies are far apart. In tuberculous meningitis the onset is gradual, and cases of sudden onset are extremely rare; in fact, I have not seen an authentic case in several hundreds of cases. In tuberculous meningitis there is a state of sopor in which some preservation of intelligence and of the surroundings exists, which does not last long, but will deepen into coma; whereas in polioencephalitis there is a diminution of the sopor, and finally after a week or two the patient is observed to be brighter.

CASE REPORTS

CASE 1.—L. D., male, aged 5 years, has had rachitis. Three years ago he had scarlet fever and diphtheria. The tonsils had been removed.

Family History.—This was negative.

Personal History.—Five weeks before admission to the hospital the patient was taken with high fever, headache and prostration. The fever apathy continued for two weeks, during which time the child vomited frequently. The fever then ran a lower course and the child became somewhat brighter, complained of severe headache, vomited occasionally, and was constipated. The patient complained of pain in the right eye and right hand. There had been no convulsions. The child was quiet but the parents thought it did not sleep. There was sighing respiration.

Examination.—When admitted to the hospital: The patient was soporose, although he answered questions. There was slight rigidity of the neck, and a tendency to yawn. There was some hydrocephalus on the right side. The reflexes were exaggerated; the pulse equal, regular, no paralyses noted of any kind. There was slight neck rigidity, *tâche cérébrale*, signs of hydrocephalus on both sides; later on the abdomen was retracted; *left internal strabismus*, patient stuporous but conscious when roused; no evident paralyses. A lumbar puncture yielded 30 c.c. of clear fluid under some pressure. A day subsequent to admission the patient was brighter. An examination of the fundus oculi revealed some small retinal hemorrhages suggesting compression of the cerebral retinal arteries but no choked disk.

Five days after admission patient was conscious with the above ocular palsy, but interested in his surroundings; some exaggeration of the knee-jerk. On walking the patient showed some tremors; complained of headache, was apathetic, pupils uneven, right larger than the left. Four days subsequently he was still apathetic and complained of headache.

A second lumbar puncture four days after the above entry yielded 40 c.c. of clear fluid under some pressure.

Two weeks after admission the patient was still apathetic, soporose, with neck rigidity, and showed slight flatness of the right side of the face.

The eyes examined by Dr. May at this time showed optic nerve atrophy, so-called postneuritic atrophy, with hemorrhage in the retina. The patient was brighter but there was still some neck rigidity and signs of hydrocephalus.

After four weeks the patient was able to be out of bed; there was some mental obtuseness, marked signs of hydrocephalus; no blindness. There was a distinct ataxia or cerebellar gait; mentality continued below the normal. The patient was up and about, without temperature and played with other children.

Puncture fluid examined showed no bacteria; 100 per cent. lymphocytes; some reaction for sugar and albumin.

The von Pirquet tuberculin reaction was negative; blood showed 12,000 leukocytes, with a differential count of 51 per cent. polynuclears on admission. On discharge, or near that, the count was 8,000 leukocytes.

The temperature was normal after the first twenty-four hours' stay in the hospital, with the exception of a rise in temperature, due to an injection of the serum of Flexner as a safeguard, should examination of the fluid show meningococci.

Discussion.—This is a typical case of polioencephalitis resembling very much a tuberculous form of meningitis—the slight rigidity, stupor, hydrocephalus and low leukocyte count. The history, however, showed an acute onset five weeks before admission to the hospital. The puncture fluid also showed fully 100 per cent. of lymphocytes, a fact which might very well be linked with tuberculosis. The child was discharged from the hospital well, however, with the remains of the encephalitis in the form of hydrocephalus and impaired mentality. The only paralysis during the illness was ocular.

CASE 2.—J. C., male, aged 7½, was admitted Dec. 22, 1908.

Family History.—Negative; no tuberculosis.

Past History.—None of the exanthemata; was perfectly healthy before the present illness; no pulmonary symptoms; bowels always normal; no urinary symptoms.

Present History.—For the previous two weeks the parents had noticed that the child had not acted as he did previously; he would cry out suddenly and then laugh; was pale; had no fever; no other symptoms until three days prior to admission when he suddenly became stuporous, cried out, complained of headache. Since then the stupor had deepened, the child almost constantly moaning and crying; no convulsions.

He had slight fever, no retraction of head, no photophobia; neck was somewhat stiff; no vomiting; bowels had been obstinately constipated; did not take any nourishment; no twisting of the face, and the child did not move its right arm as well as its left; occasionally cried out at night; with grinding of the teeth.

Physical Examination.—Fairly well nourished, lay in a stuporous condition; head somewhat retracted, patient constantly sighed and moaned with grinding

of his teeth; restlessness during examination; seemed unable to move the left arm and leg, respiration was very irregular; practically no rigidity of the neck; some Macewen, especially on right side of the head; *tâche* present; no Kernig, no hyperesthesia, slight photophobia. Mucous membranes normal; no ataxia; no herpes; ears negative; eyes, both upper lids somewhat ptosed, pupils equal, regular, reacted to light; eyes had a slight nystagmus-like motion; no strabismus; conjunctivæ somewhat injected; no petechia; some excoriation about the alæ nasi; teeth and gums in fairly good condition; sordes on lips; tongue coated. Posterior cervical and a few small axillary glands enlarged. Examination otherwise negative; chest fairly well formed; lungs negative; heart normal; action somewhat irregular and rapid; no murmurs; abdomen retracted, lax, no pain; normal; liver normal; spleen negative.

Extremities: Right arm somewhat spastic, hand held clenched, and, as noted above, the child was inclined to move left extremity more than the right; knee-jerks exaggerated. No Babinski, no ankle-clonus.

December 23 lumbar puncture; 33 c.c. of clear fluid under moderate pressure removed; tuberculin cutaneous reaction negative. White blood cells 10,000; 64 per cent. polynuclears.

December 24. General condition somewhat better; less irritable, lay in a semistuporous condition; eyes slightly rotated to the left; no rigidity of neck; no Kernig. Second tuberculin reaction negative.

December 25. Examination of the eyes negative.

December 27. General condition fair; still irritable; did not speak; rigidity of the neck; no signs of hydrocephalus; pupils equal; knee-jerks exaggerated; left tendon reflexes exaggerated; physical condition the same.

December 28. Lumbar puncture; 20 c.c. of clear fluid removed.

January 1. The patient for the previous few days had had periods of stupor and maudlin delirium, in which he cried in a low tone; did not answer questions; did not seem conscious of his surroundings; no paralysis of the extremities, with the exception of the right upper extremity, which seemed to be weaker than its fellow; patient turned his head from side to side constantly; did not take nourishment; no signs of nuclear involvement in the shape of paresis or paralysis.

January 2. Tuberculin reaction negative; general condition much improved; very noisy and delirious most of the day; had a hot bath and then became brighter; seemed to see and hear when spoken to, but did not speak; he motioned with his hands. Very noisy the previous night; took nourishment better; lungs and eyes negative; no paralysis; moved the left arm more than the right; knee-jerks exaggerated.

January 6. The patient in the morning was conscious; sat up in bed with a meaningless smile, when he talked speech was indistinct; had a nasal timbre. Patient did anything he was told to do; had marked loss of power in upper and lower extremities; had a Romberg; when he stood or walked he staggered; his arm and fingers taking on position of athetosis; had no paralysis or paresis of facial muscles; expression of eyes rather vacant, but was conscious and brighter.

January 9. Patient much quieter and brighter, had at times an idiotic smile; speech somewhat indistinct, and had a nasal tone; slight flatness of right side of face; tongue deviated slightly to the right; pupils central—reacted to light; right grip not as strong as left; no apparent atrophy, used arm fairly well; the right leg was quite as strong as the left; knee-jerks active; otherwise negative.

January 16. Discharged well; no paralysis; bright; speech still somewhat nasal.

The temperature the first week, from December 21 to 28, ranged from 98.5 to 99.8 in the rectum. After that it remained normal for four weeks, when he was discharged.

The urine was examined three times during the stay in the hospital and was found negative. The lumbar puncture fluid was examined twice.

January 2, Cytology, 100 per cent., lymphocytes; bacteriology, negative; traces of albumin. The second specimen 50 c.c.; report of sugar reduction; 95 per cent. lymphocytes; mononuclears; no bacteria. Pathologist thought it had more the character of a transudate than an exudate.

Discussion.—In this case there is an imperfect previous history in that no sudden onset with fever was obtained, but there was a period of two weeks of mental irregularities, slight fever and increasing sopor. The patient on admission to the hospital was unconscious and delirious. This delirium was of a distinctly maudlin variety and cleared up completely, leaving a bright intellect. There was on admission, also, rigidity of the neck, vomiting and headache. There was no real paralysis or strabismus. The reflexes were increased. There were signs of internal hydrocephalus. In this case there was a distinct marked leukocytosis, 30,000, with a polynuclear blood-count of 88 per cent. The puncture fluid also showed a lymphocytosis of 100 per cent. and 95 per cent., sterile to culture; some albumin and sugar. There was during the course of the affection slight flatness of one side of the face, some slight deviation of the tongue, and a nasal timbre to the voice. The latter persisted until his discharge.

CASE 3.—J. H., aged 4½, was admitted to the service March 2, 1909.

Family History.—No tuberculosis; the stepmother had a cough and hematemesis and saw the child frequently.

Previous History.—No measles, scarlet fever, pertussis or diphtheria; at the age of 6 months the patient had pneumonia for five days.

Present Illness.—This began five weeks prior to admission with occasional vomiting, which increased in frequency until the child vomited after each meal. No vomiting occurred in the previous two weeks. At that time the child complained of headache and pain in the abdomen, and continued to complain of headache up to admission; had marked cough for a short time two weeks prior to admission and began to be drowsy and slept a good deal of the day; was conscious and recognized mother and asked for food, and played with her toys until five days prior to admission, when she developed rigidity of the neck. For the previous five days the child had seemed to be brighter and had remained in bed, up to that time she was up and about; *she did not seem to see well.* No fever or paralysis; the bowels were constipated; history of low temperature; no febrile movement.

Physical Examination (by house physician).—General condition poor, though fairly well nourished; marked rigidity of neck with Macewen; no Kernig; *tâche cérébrale* present; patient lay in a stuporous condition; could not be roused;

made motions with the hands, did not talk; no hyperacusis, no photophobia; somewhat irritable when disturbed; no eruption on the skin; the ears were negative.

Eyes.—Left pupil larger than the right; they reacted to light; conjunctivæ negative; left internal strabismus; no facial paralysis; teeth and gums in fair condition; tongue coated, moist; throat slightly red; larynx, trachea, and thyroids negative; a few axillary glands could be felt; chest fairly well formed; otherwise negative; heart negative; abdomen negative; liver also; spleen not felt; genitals negative, with slight discharge; no edema of the extremities; knee-jerks exaggerated; there was ankle-clonus on both sides; there was a Babinski on left side; no paralyses.

Synopsis.—Stupor, irritability, rigidity, Macewen, *tâche*, ankle-clonus, Babinski, exaggerated knee-jerks, left internal strabismus.

March 3. Lumbar puncture; 30 c.c. of clear fluid containing flocculi was removed. Blood examination: Leukocytes, 30,000, polynuclears 88 per cent. Fundi of eyes examined; negative.

March 5. General condition about the same, patient was in bed; stuporous, but could be roused and then was irritable; moderate retraction of head, marked rigidity of neck, Macewen, slight Kernig; *tâche* present; slight weakness of the left external rectus; no paralysis nor paresis; did not void urine; must be catheterized. Respiration cerebral; no clonus, no Babinski.

March 7. Patient was irritable when disturbed; quiet when left alone; had a Kernig, rigidity of neck, Babinski, no Macewen; cries out. Lumbar puncture; 33 c.c. of clear fluid obtained; contained flocculi.

March 10. Patient was conscious; irritable and disposed to cry; sat up in bed when not watched; noticed everything around the bed. Slight Kernig with Babinski, especially on right side; rigidity of the neck; took nourishment; fundus of the eye normal.

March 12. This a. m. the patient was noisy; had distinct retraction of head; rigidity, Kernig, Babinski, opisthotonos; no paralysis of the facial muscles; took nourishment fairly well; was conscious; pulse slow and regular. White blood cells, 12,200; polynuclears 71 per cent.

March 14. Patient was more rational; sat up in bed; no paralysis; there was slight rigidity of neck, slight Kernig, no Macewen; chest and abdomen negative; took nourishment quite well; tuberculin reaction negative.

March 15. Improvement continued; patient sat up and noticed objects; was less irritable; had slight internal strabismus on the left side.

Patient's general condition was good; was more conscious; more or less aware of surroundings, no rigidity, no Kernig, slight Macewen on left side, no paralysis of limbs. Weakness of the left internal rectus.

March 17. Patient was examined with reference to paralysis; none of the face and extremities was found; strabismus still noted.

March 28. Patient had been up and about the last week; had only a left internal strasbismus left. Discharged.

During the patient's stay in the hospital the temperature ranged from 98 to 100.8 F. in the rectum during the first week, and then fell to normal; pulse and respiration ranged from 20 to 30 for the latter to 90 to 136 for the former, the latter during the fever. When she was up and about the patient's pulse and respiration were 80 and 24 respectively.

The night nurse noted that during the first week the patient slept fairly well, but cried out at night and was restless at times; it was necessary to catheterize

the patient; but after March 6 the patient, though restless, slept fairly well without any delirium. The urine examined during the patient's stay in hospital was negative.

The cerebrospinal fluid examined was negative on first puncture as to bacteria; there was a slight amount of albumin present and some sugar.

The second lumbar puncture, March 10, gave a cytology of mononuclears of 98 per cent., with no bacteria to culture or to spread; there was some albumin, 2 mg., and no sugar.

Discussion.—I saw this case in consultation. The onset was more or less acute. The subsequent history resembled a tuberculous meningitis, and the diagnosis was placed as a probable instance of this disease. In the hospital the symptoms cleared up, so that the patient, who was exceedingly bright, was up and about after two weeks. It is to be noted after discharge that though the patient's eyesight was good she returned in a month with a history of blindness of sudden onset. This, after a while, cleared up so that the patient could discern objects clearly. The fundus showed an optic atrophy. In the course of the affection there was a blood leukocytosis of 30,000, with a polynuclear count of 88 per cent. The fluids obtained by lumbar puncture gave a lymphocytic cytology of 98 per cent., some albumin, no sugar. The urine was negative; as also the lungs. Repeated von Pirquet skin tuberculin test was negative, and the temperature for the stay in the hospital did not exceed the normal after the first week. This case so closely resembled a tuberculous meningitis that a differential diagnosis without prolonged observation seemed impossible.

CASE 4.—S. F., schoolgirl, aged 11, was admitted to the hospital Feb. 8, 1909.

Family History.—Seven other children living and well. No history of tuberculosis.

Previous History.—Measles, no scarlet fever, no pertussis, no diphtheria, occasionally sore throat, no rheumatism, no pneumonia, no other complaint.

Ten days prior to admission the patient was taken ill and was in bed with high fever, vomiting, headache, malaise; then patient was up and about, but complained of occasional headache until February 7.

Present Illness.—The day before admission she had severe headache, and began to vomit; this continued until the day of admission, when she had general convulsions. Starting with a severe convulsion she had passed into a state of unconsciousness with some fever. The convulsions were repeated and back and neck became rigid; the bowels were constipated; there was no cough or vomiting on day of admission to hospital.

Physical Examination.—(By house physician.)—General condition fair; patient well nourished; slight soporose condition; patient continued to lie on the left side; conscious; irritable; there was some rigidity of the neck; marked Macewen; slight Kernig; *tâche cérébrale.* Patient could be roused from soporose condition; did not seem to be conscious, but simply moaned and cried; respiration

somewhat irregular; cheeks flushed; put hands to head at times; twitching; no retraction of the head. The skin showed some flea-bites, *"tâche bleuatre;"* no petechia; ears and mastoid negative; pupils regular; central, easily dilated; conjunctivæ injected; no paralysis; there was sordes in mouth; teeth and gums in good condition; tongue was coated and moist; throat showed muco-pus; no facial paralysis; thyroids and spine negative; few small axillary and inguinal glands to be felt; chest negative; somewhat sunken; abdomen retracted; liver, spleen and genitals negative. Extremities: Slight edema over the tibias; knee-jerks not obtained; no Babinski; no paralyses.

Synopsis.—Stupor, Macewen, Kernig, rigidity of the neck, *tâche cérébrale.*

February 9. Lumbar puncture; 35 c.c. of clear fluid removed under great pressure, and 30 c.c. of Flexner serum injected as a precaution should meningococcus be present on examination. White blood cells, 72,000; polynuclears, 79 per cent. Cutaneous tuberculin reaction negative.

February 10. Patient lay in a crouched position; was irritable when disturbed; cried out and was exceedingly hyperesthetic; retraction of head, rigidity, Kernig, as on the previous day; arms and extremities showed some edema still present; patient had ordinary redness of fauces; chest negative; patient did not take nourishment.

February 11. Patient had a general exanthematous rash (serum); patient lies in same position as on the previous day; general condition about the same; delirious when disturbed; rigidity and Kernig still present. Nurse reported that patient sat up and took notice of things.

February 12. The patient was much improved; opened her eyes and seemed to notice objects; was much clearer and did not resist quite so much. There was still very marked Kernig and very marked rigidity of the neck and retraction of head; there was also mydriasis when the head was flexed and slight strabismus on the left side.

February 13. When the patient was admitted the urine was of a distinctly brownish tint; it had now become clear but was distinctly colored; estimate of urine very difficult on account of the involuntary discharges; patient when left alone was very quiet; when interfered with still resisted; did not answer questions. Patient seemed to be more conscious, but was apparently deaf; no paralyses; Kernig still present.

White blood cells, 12,000; polynuclears, 83 per cent; fundus of the eyes normal.

February 14. Patient the previous night sat up; was quite logical, but apparently deaf; when any one came near her the patient was frightened, but was more rational than the previous day; no edema of the tibia. There was a Kernig, rigidity of the neck, no Macewen, excretions involuntary.

February 15. Patient could hear; was more rational; had external strabismus of right eye; this was noted the previous day; rigidity of neck still present; as also Kernig; had normal reflexes on both sides; some edema of the tibia.

February 16. Patient improved; more rational; Kernig and rigidity still present; the urine was normal.

February 17. Patient sat up; was quite rational; external strabismus of the right eye unchanged; Kernig still present; headache of the day before was gone.

February 19. The patient continued to improve; no apparent paralyses of the extremities; no paralysis of facial muscles.

February 22. The patient complained of lack of power of left hand; right grasp a little stronger; no limitation of motion of upper extremities; no apparent atrophy.

February 24. Slight limp in left leg, knee-jerks on left side diminished.

February 25. Patient looked bright; felt well; slight Kernig; slight weakness of left upper extremity.

March 2. Patient examined to-day; appeared bright and normal; slight loss of power in left hand; no atrophy of muscles visible in upper and lower extremities; no loss of power; no Kernig; no Babinski; no ocular or facial paralyses. Patient had loss of power in left arm, but this was more apparent than real.

The temperature of the patient, which from admission February 8 to February 14 ranged up to 104 F., gradually fell on February 14 to 100 F.; respiration became pretty regular—from 22 to 32—and the pulse was 90 to 120. The following day the temperature, pulse and respiration were normal.

The night nurse reported that on admission and at intervals afterward the child was particularly noisy at night. During the day she was quite comfortable. The urination was almost always involuntary. She refused nourishment, was constipated up to February 12, after which time she slept at night and was quiet. The puncture fluid was reported as practically normal; there was sugar present, also traces of albumin; cytologic examination showed a few mononuclear cells. Wassermann was negative. The urine was obtained by catheter and, with the exception of a few bacterial cells, was sterile.

Examination of Urine.—February 11, hyaline and granular casts, and some blood and pus were present. February 12, about the same—blood, pus and casts. February 14, a few granular casts. February 15, no casts and no blood; negative after that time with the exception of a few leukocytes.

Discussion.—In this case the onset was acute, there then was a remission in symptoms and then the patient took to bed after a week with all the symptoms of a meningitic attack; in fact, when seen in consultation a cerebrospinal meningitis was suspected, and a puncture was made with that diagnosis in view, but the fluid obtained was clear and nothing found but a lymphocytic cytology. There was a high leukocyte count of the blood, including an excess of polynuclear cells. The illness ran the course of an acute meningitis. The finding in the urine corresponds to that of Wickman in one of his cases. Inasmuch as the urine cleared up completely, it must be surmised that the nephritis was only part of a general infection. The patient fully recovered, with a strabismus due to ocular palsy remaining with slight weakness in the left upper extremity. This, I think, is a case of acute polio-encephalitis with a meningitic onset, its course closely simulating cerebrospinal meningitis of the epidemic type. The patient was not discharged until she had absolutely recovered.

CASE 5.—Female, aged 5, was admitted Oct. 14, 1909.

Family History.—Father suffered from pulmonary tuberculosis; mother and nine other children healthy.

Previous History.—The patient was born at full term; no instruments used; measles at 2½ years; no complications; whooping-cough just previous to measles.

The patient had a moderate dry cough since having measles up to one year prior to admission. No convulsions, no ear symptoms, bowels regular, urination normal. About sixteen months before admission the patient was operated on for acute appendicitis; ill five weeks; healthy since until present illness.

Present Illness.—Present illness began four days prior to admission, when the mother noticed that the child became drowsy, lost interest in her surroundings and developed moderate fever. The next day the child vomited for the first time. The vomitus consisted at first of undigested food; later of small amounts of bile-stained fluid, accompanied by much retching; vomited since, chiefly after taking food.

Since the onset the bowels were obstinately costive; no marked abdominal distention, no blood or mucus in stool. Drowsiness became intensified; child would start in her sleep with a shriek; sighed considerably. The day before admission the child complained of pain in back of neck, developed some rigidity and became delirious and irrational; no convulsions, no palsies, slight dry cough, no dyspnea; marked prostation; drowsy; responded when disturbed; was irrational and delirious; respiration irregular; no head retraction; neck was rigid; general hyperesthesia; Macewen present, especially on left side; marked photophobia. Eyes, ears and mastoids normal; skin showed scar of operation; *tâche cérébrale* present; scattered papular spots; a few small lymph-nodes in left axilla; tongue, dry and coated; throat, teeth and gums in good condition; chest well formed; lungs clear; heart borders normal; action regular, rapid, of poor force, sounds clear, no murmurs; pulses equal, regular, rapid, small.

Liver and spleen not enlarged; abdomen lax; reflexes present.

Extremities.—Kernig's sign present on left side; left, Babinski at times.

Synopsis.—Fever, drowsiness, delirium, hyperesthesia, rigidity of neck, Macewen, left Kernig.

Blood Count.—White blood cells, 21,000; polynuclears 61 per cent.; small lymphocytes 28 per cent.; large lymphocytes 11 per cent.

October 15. Lumbar puncture; 24 c.c. clear, colorless fluid under increased tension withdrawn.

October 16. This morning patient was semiconscious; roused when talked to; athetosis in hand; dry, coated tongue; talks with lisp; slight flatness of left side of face; Kernig on both sides; marked rigidity and tenderness of neck; slight Macewen on left side.

October 17. Lungs negative; paresis of left side of face more marked; marked rigidity of neck; marked Kernig on both sides; fundus examination of eyes was negative; patient semiconscious. Von Pirquet positive.

October 18. More conscious; Kernig; Macewen very slight on left side; slight internal rotation of left eye; marked neck rigidity.

October 23. Von Pirquet still evident; Kernig, left facial flatness; bromic eruption on legs; could sit up; rigidity of neck almost gone; tongue moist; Macewen not elicited.

October 24. Urine amber, acid, specific gravity 12, albumin 0; a few white blood cells.

October 25. Sat up; left side of face still slightly flat; neck supple; Kernig, 30 degrees on both sides.

November 4. Urine amber, acid, specific gravity 24, albumin 0; a few white blood cells.

October 15. Cerebrospinal fluid showed lymphocytes 100 per cent.; negative for bacteria; no growths; no tuberculosis; albumin .5 mm.; sugar reducing substance present; Widal negative 1 to 20, 1 to 50; also on October 18.

October 14. Temperature 104.2 F. on admission; dropped to 100.8 F. on following day; and on sixteenth reached 99 F.; slight rises to 100 F. afterward. Pulse 116 on admission, respiration 28. Weight 45¾ pounds.

Discussion.—This patient, 5 years of age, was attacked more or less acutely with high fever and vomiting, passed into a condition of sopor which became intensified after a few days. There was the picture of meningitis with fever, drowsiness, delirium, apathy, vomiting, constipation, pain in neck and rigidity of the neck. What was especially disquieting was a positive von Pirquet cutaneous reaction to tuberculin, which misled into the diagnosis of tuberculous meningitis. The subsequent complete recovery disproved this, leaving us to infer a latent glandular tuberculosis. The fluid obtained by lumbar puncture showed nothing more than a marked lymphocytosis.

The recovery of this patient was complete, there being left only a slight facial flatness; no real paralysis. The temperature after the first day following admission to the hospital was normal; the urine was normal; the fundus oculi was normal.

CASE 6.—This case resembles a case I saw recently in consultation, a girl of 13. The girl was seen by several physicians, all being quite positive in the diagnosis of tuberculous meningitis. This girl like the case I am to depict recovered, with the exception that she did not, as in this case, yield a positive tuberculin reaction.

History.—The patient was a boy, aged 4, admitted to my hospital service. He had had measles, scarlet fever and diphtheria.

Present Illness.—This began three weeks before with an attack of fever and vomiting and headache; following this the boy became drowsy, did not notice and was soporose and stupid. The condition of drowsiness became more and more marked, and in this condition he was brought to the hospital. The patient was well nourished, had some slight hydrocephalus, staggered when upright, swayed especially to the left when he walked and threatened to fall. The patient was in a trance-like state and sat up in bed staring ahead; he slept well. The examination of the fundus oculi was negative.

The patient's urine at first contained acetone, diacetic acid and a trace of sugar. These disappeared in the first two days of the hospital stay. After three weeks of illness the above symptoms cleared and the patient was well. There was from the first a positive tuberculin skin reaction (von Pirquet). No lumbar puncture was made. This case differs from that of the girl I just mentioned, inasmuch as the latter had no tuberculin reaction and was unable to sit up or stand without experiencing marked vertigo. The girl was highly hyperesthetic, whereas this symptom was absent in the boy.

CASE 7.—C. R., aged 5½, was admitted Jan. 10, 1911.

Family History.—Negative.

Previous History.—Had pneumonia and measles one year ago; no other diseases. The child was perfectly well until thirteen days before admission.

Present Illness.—This began thirteen days previously with vomiting and headache. The child vomited one to three times practically every day since onset; vomiting was not projectile in character, having no relation to meals. Headache had been frontal in location and almost constant in character; had slight fever following the onset; for a week had occasional cough, with slight mucopurulent expectorations. For two days the father noticed that the child had been drowsy most of the time, and was rather irritable when awakened. There were no disturbances of the special senses; no paralyses noted; no ear disturbances; bowels fairly regular; urination normal; appetite poor; no symptoms of cardiac or renal disturbances.

Synopsis.—Vomiting and headache for three days, slight fever, slight cough; drowsiness for two days.

Physical Examination.—General condition good; well nourished; irritable. Head—no rigidity, no Macewen. Eyes—pupils equal; react to light and dilate, no palsies. Ears and mastoid negative. Mouth and teeth—several upper teeth missing; otherwise in fair condition; tongue moist and coated; throat congested. Glands and skin negative; chest well formed, expansion good; lungs negative; heart, regular, good force, no murmurs; liver—fifth space, sixth rib to free border; not felt; spleen not felt. Abdomen held tense; tympanitic; no masses; abdominal reflexes not obtained; slight *tâche.*

Extremities.—Knee-jerks much exaggerated; no Kernig, no clonus; Babinski and Oppenheim, bilateral; patella-jerk bilateral; tremor of upper extremities.

Genitals.—Some reddening of vulva; no discharge. Rectal examination not made.

Synopsis.—Irritability, exaggerated knee-jerks, Babinski, Oppenheim, tremor of upper extremities.

January 11. White blood cells 31,200; polynuclears 80 per cent.; lymphocytes 18 per cent.; large mononuclears 1 per cent; basophils 1 per cent.

January 12. Ears negative. Lumbar puncture made; about 30 c.c. of clear fluid and flakes withdrawn.

January 13. White blood cells 21,200; polynuclears 80 per cent.; lymphocytes 14 per cent.; large mononuclears 5 per cent; easinophils 1 per cent.

January 16. General condition better; child brighter; slight rigidity of neck persists; no Kernig.

January 22. Inner reflexes present; child will not stand; eyes closed; uncertain gait present.

January 24. Child had been picking up but complained of pain in extremities; reflexes increased; Kernig present; resents interference; no pain in back; no headache.

White blood cells 10,600; polynuclears 73 per cent; small mononuclears 26 per cent.; large mononuclears 1 per cent.

February 7. Patient up and about ward.

The temperature during the first week of the hospital stay ranged from 99 to 101 F. and then dropped to the normal.

Urine during stay in hospital at only one time showed a few hyalin casts.

The fluid obtained by lumbar puncture contained 90 per cent. lymphocytes and 10 per cent. polynuclear cells. Smears and culture negative as to bacteria; sugar, moderate reduction; some albumin.

Discussion.—The onset was sudden, with headache and vomiting daily, slight fever with cough, and after ten days, increasing sopor and irritability. On admission to the hospital there were no palsies, but there was the mental irritability, exaggerated reflexes with tremors of the extremities. The blood showed during the illness a marked polynuclear leukocytosis with a lymphocytic picture in the spinal puncture fluid.

I have thus described a condition which is of great interest. It is apt to be, and is constantly, mistaken for meningitis of the cerebrospinal, acute suppurative or subacute tuberculous form. The onset of the illness is acute; it begins with a previous history of absolute health. After the acute symptoms set in there may be in some cases an abatement and then a recurrence of symptoms of a cerebral nature, which gradually deepen. If the case is one resembling an acute meningitis, the symptoms are more active, with neck rigidity, pain in the neck, headache and delirium. If the case resembles the tuberculous form of meningitis, the patient lies more quietly, exhibits palsies of the cranial nerves, and may even have marked hydrocephalus with distinct Cheyne-Stokes respiration and unconsciousness. In both sets of cases the delirium, sopor or coma lightens, the patients after a week or more of illness become brighter, and recovery proceeds. Lumbar puncture in all the cases reveals a clear or slightly flocculent fluid, without bacteria, and a cytology of 90 per cent. to 100 per cent. lymphocytes. An examination of the blood shows at first a leukocytosis of pronounced degree of the polynuclear type.

The onset of the disease may be ushered in by fever, which rapidly subsides to within a fraction of a degree of the normal and the major part of the illness runs its course with this temperature, which is practically normal. The diagnosis is made from the points of clinical course laid down in this paper. The prognosis is for the most part good, except in those cases which involve the nuclei of the nerves controlling respiration. In such cases the outlook is that of an acute bulbar paralysis, when the extent of the lesion will decide the fate of the case. The main point is to have in mind the great similarity of a certain set of these cases to those of tuberculous meningitis, and acute cerebrospinal meningitis, and the absolute futility of a positive diagnosis without study of the case, lumbar puncture and all the clinical aids at our command.

The fatal cases of the cerebral forms of polioencephalitis have been mentioned in this paper. I have two cases of this kind to report, in one

of which autopsy was performed and the diagnosis of polioencephalitis confirmed. These cases may be of sudden onset with cerebral symptoms, and a rapid involvement of the bulbar nuclei. The result is a picture of acute bulbar paralysis with cerebral onset. In some cases the onset may be gradual, in others acute. The paralysis involves the muscles of deglutition and phonation and this is the first sign of bulbar involvement of a serious nature. In these cases the ocular and facial nuclei may be involved, and as the process spreads down there is a complete paralysis of a descending type, involving the muscles of respiration. In one of the cases the respirations seemed to cease first while the heart continued beating. All cases here recorded were fatal cases, but this must in no way be assumed to be always the case, because I have seen a few bulbar cases recover, one notably in a child 3 years of age, in which the respiration was involved, as was also deglutition. In this case a complete recovery occurred.

CASE 8.—A. B., male, aged 5, was admitted Oct. 4, 1908.

Family History.—Father had tuberculosis in 1905 when at Bedford Station; since then was well. He had lost 5 pounds in the previous few weeks. The mother and two other children were well.

Previous History.—The patient had measles two years ago; otherwise no illnesses; bowels always regular; appetite good; mentally bright; never complained of headache; eyes and ears good; no eruptions on skin.

Present Illness.—Onset one and one-half weeks prior to admission, with indefinite symptoms. It was noted that the child was weak and lackadaisical; did not complain of headache; had no convulsion or palsies; had some fever; appetite was good; child slept uneasily at night and cried out in sleep; bowels regular; in the previous four days the child began to cough when talking; had difficulty in swallowing; regurgitation and coughing back food mixed with mucus; had been unable to talk in this time; unable to sit up or walk; ears and eyes remain functionally unaffected; complained of slight pain over heart; cried out frequently in sleep and had involuntary movements of arm.

Physical Examination.—General condition fair; patient well nourished; lay in an apathetic condition; cheeks flushed; moderate dyspnea; child was hoarse; marked gurgling in throat; alæ nasi dilate with each inspiration; child responds when spoken to; voice thick and husky; moderate rigidity of neck; on bending neck child was irritated; Macewen on left side; no irregularity of skull; no definite tenderness made out; no retraction of head; child somewhat irritable; Kernig; *tâche cérébrale* present; moves arms and lower extremities, but acts as if in trance; answers monosyllabic.

Skin and mucous membranes had a good color; ears and mastoids externally negative; moderate amount of cerumen in canal; eyes and upper lids somewhat closed so that upper one-half of pupil was covered. This could be overcome and child raised lid in normal manner. Pupils: right slightly larger than left. regular, central moderately dilated; reacted somewhat sluggishly to light and accommodation; weakness of both external recti; conjunctivæ negative. Nose—evidences of slight secretion ali nasi; otherwise negative. Face—left-sided facial

paresis. Mouth, teeth and gums in poor condition; tongue thickly coated and moist; tonsils hypertrophied. Throat—uvula elongated; throat slightly ingested; palate moves slightly. Larynx, trachea, thyroid, spine, bones and joints negative; a few small cervical and inguinal glands were palpable.

Chest was well formed and symmetrical; right chest seemed to expand slightly more than left; no retraction.

Lungs: Anteriorly there was some dulness over the right axilla; marked bronchial râles over entire chest; breathing over anterior chest was exaggerated; numerous loud gurgling râles and expirations which seem to be transmitted from trachea. In the right axilla there were a few mucus râles on inspiration; posteriorly there was dulness at right apex down to about two fingers below spine; dulness at left apex of similar extent; over entire chest posteriorly there were numerous bubbling râles on inspiration and expiration; most marked at left base; breathing harsh and exaggerated; no change in voice.

Heart: Right border at right border of sternum; left border in nipple line; visible beat at fourth rib; apex neither seen nor felt; sounds clear; no murmurs; action regular; good force; somewhat accelerated.

Abdomen: Somewhat retracted and lax; no pain or tenderness. Liver, fifth rib to sixth rib; free border not felt; spleen not felt.

Extremities: Upper, grips seem to be equal; child seems to use left hand more than right, although both can be used fairly well; right arm weaker than left; no impairment on passive motion; no atrophies; arm reflexes present. Lower slight edema; knee-jerk not obtained; no clonus; no Babinski; no paresis or paralysis of legs.

Genitals: Double cryptorchidism. Rectal examination not made.

Blood: Leukocytes 25,000.

October 15. Eyes examined and found negative.

The child's condition remained about the same; lay quietly, preferably on the right side; child gets frequent attacks of dyspnea, which were accompanied by loud breathing; on auscultation there were found numerous moist gurgling râles throughout the chest; child takes nourishment very poorly, owing to the difficulty which it has in swallowing; reflexes in extremities gone.

October 16. Condition remained the same; lay quietly; eyes half open; had some photophobia and could see objects readily; had slight weakness of the external and internal recti muscles of the eyes; could not swallow; regurgitated all food given by gavage; breathing remained the same; signs of pulmonary edema came on frequently and cleared up in a large measure after hyperdermic injection of atropin. It was necessary to resort to rectal feeding. Lower extremities had no reflexes; abdominal reflexes also gone; there was no Kernig; electrical reactions and sensations not yet tested.

Blood: Leukocytes 33,000.

Urine: Hyalin casts; few granular casts.

The patient died with signs of respiratory failure. Postmortem made.

CASE 9.—G. R., female, admitted November 4, 1910.

Family History.—Seven other children, all well; father coughs; no tuberculosis.

Previous History.—The patient had measles; no other disease; no cardiac, pulmonary or renal disease, no rheumatism. Previous to present illness the child was perfectly well and played about in the street.

Present History.—At 5 o'clock a. m. on the morning of admission the child had involuntary urination while in bed; on taking her up she squirmed about and

screamed; it was then noticed that the child could not articulate and could not stand on its feet; vomited once in the morning, and whenever she was given anything to eat; appeared to have some difficulty in swallowing; all day the child lay quietly in bed without moving a limb; had no fever.

Physical Examination.—General condition good; patient well nourished; flushed facies; markedly apathetic; somewhat stuporose; respiration somewhat rapid and regular; does not cry nor give response to spoken language; neck, no rigidity, no mastoid; Macewen present; distinct flatness of right side of face; right palpebral fissure not completely closed; mouth drawn to the left.

Eyes: Pupils equal, central and regular; mucoid discharge from conjunctivæ; no corneal anesthesia; no petechia or palsies; dry crusting of nose; lips of good color; tongue somewhat coated; gums in good conditions; teeth in good condition; pharynx negative; palate, slight deviation to left; moves actively; skin, clear, good color; one or two small healing scars.

Glands: Submaxillary, post cervical, chains.

Chest: Well shaped; lungs, negative; heart, borders not enlarged; apex, fourth space within nipple line; action rapid and regular; pulse, equal, regular, rapid.

Abdomen: Negative; liver, fourth to sixth ribs; spleen not felt.

General: Patient unable to hold back up; head falls weakly to side; weakness of right side of body complete; right arm useless; left knee-jerk just present; left arm tendon reflex exaggerated; right knee reflex elicited with difficulty; right arm completely relaxed; apparently no power; slight redness of vulva.

November 6. Patient in a condition of apathy; the Macewen still quite marked, more so than the previous day; right facial paralysis marked; a little weakness of external rectus of right side; complete right hemiplegia; knee-jerks absent on paralyzed side; present on left side; considerable atrophy of the right deltoid, biceps and triceps; sighing respiration; *reaction of von Pirquet 2 mm. positive;* slow, forcible heart action; child vomited once; constipation present; swallowed with difficulty; refused nourishment; did not talk; a little lagophthalmus of right eye.

November 4. Von Pirquet; white blood cells 17,600; polynuclears 82 per cent.; small lymphocytes 16 per cent.; small mononuclears 2 per cent.

There was a slight difference in size of the thighs, the affected being smaller; exaggerated reflex of left affected extremity; only occasionally obtainable on right side; weakness of the muscles of the neck; head fell back; child could sit up.

November 6. Right knee-jerk this morning easily obtainable; left knee-jerk elicited with difficulty; left triceps-jerk exaggerated; right not obtained.

November 7. Heart continued beating after respiration ceased. Temperature ranged from 100 to 104.8 F.; at death 102.5 F.; pulse 96 to 130; respiration 24 to 36.

Fluid obtained by lumbar puncture: First puncture had lymphocytes too few to count; no bacteria; animal inoculated. Second puncture: Cytology, 72 per cent. lymphocytes, polynuclears 28 per cent.; negative to bacteria; albumin 1 mm.; sugar, slight reduction.

Blood culture, negative.

30 East Sixty-Second Street.

INFANTILE PARALYSIS: SPINAL FORM

JOHN LOVETT MORSE, A.M., M.D.

It hardly seems necessary to consider in detail the symptomatology of the ordinary classical type of the spinal form of infantile paralysis. Everyone knows how varied the onset may be and how much difference there is in the severity of the constitutional symptoms. It is common knowledge that the paralysis comes on quickly in the course of a few hours, or at most in three or four days; that there is then a stationary period of from one to four weeks, which is followed by a period of improvement lasting from six months to perhaps a year, and that the final paralysis is always less than the initial. The improvement in the paralysis is due to the facts that many of the ganglion cells, which at the height of the disease are merely compressed or only partially involved, recover their function, wholly or in part, and that the nerve-supply of a muscle never arises from a single segment of the cord.

It is impossible, therefore, in the acute stage to prophesy how extensive the final paralysis will be. Recovery is sometimes nearly or quite complete when the initial paralysis is very marked, while at other times there is very little improvement, even when the original paralysis is slight. On general principles, however, the greater the extent of the initial paralysis, the later the beginning of the stage of retrogression and the slower its progress, the greater is the final paralysis.

The final paralysis is, as a rule, monoplegic or hemiplegic, seldom diplegic or paraplegic. It seems idle, however, to give statistics as to the relative frequency with which the different extremities are involved or to detail the possible combinations, because these facts are of no practical importance in the individual instance. It is comparatively unusual, however, to have all the muscles of an extremity involved or, at any rate, involved to the same extent. In most instances some of the muscles are spared and in many only one or two are affected. The grouping of the paralyzed muscles has, moreover, no relation to their physiologic function, the distribution of the paralysis in many instances appearing most peculiar. The peculiar distribution of the paralysis is easily understood, however, when it is remembered that the nerve-supply of a given portion of an extremity, the forearm, for example, does not all arise at the same

level of the cord, that the blood-supply of the cord is horizontal, not vertical, and that the affection of the cord is due to interference with the blood-supply, resulting from inflammatory processes in the vessel walls, due to infection originating in the subarachnoid space.

It is not very unusual for other muscles than those of the extremities to be involved, while these escape. Such muscles are most often the erectors of the spine and the abdominal muscles. The involvement is, moreover, not infrequently unilateral. The paralysis is, for example, sometimes limited to the extensor muscles of the neck, to the muscles of one side of the spine, or to those of one side of the abdomen. Paralysis or paresis of these muscles is often overlooked and the deformities to which they give rise attributed to other causes. Scoliosis from this cause is very often misinterpreted and enlargement of the abdomen from paralysis of the abdominal muscles is attributed to indigestion with flatulence, or to ascites. In one patient whom I saw, a unilateral paralysis of the abdominal muscles had been mistaken for an abdominal tumor. Incidentally, the prognosis in paralysis of the abdominal muscles is fairly good.

THE PROGRESSIVE TYPE

In a certain number of instances the paralysis is of the progressive type. It usually begins in the lower extremities and gradually extends upward, resembling in its course that of the so-called "Landry's paralysis." It is probable, in fact, that a very considerable proportion, if not all, of the cases which have in the past been described under this name were really cases of infantile paralysis. When the paralysis reaches the external muscles of respiration, as it not infrequently does in this type, a fatal outcome is practically inevitable. In certain cases the phrenic nerve is also involved. Death occurs sooner, of course, when this happens. This form must not be confused with that in which death results from respiratory paralysis due to the involvement of the centers of respiration in the medulla. In other instances the paralysis begins in the arms and extends both downward to the lower extremities and upward to the centers in the medulla.

THE POLYNEURITIC TYPE

Pain is a prominent symptom in many instances. It is, in fact, so common that it is hard to understand how the old dictum that there is no pain in infantile paralysis ever originated. The pain is sometimes in the joints, but more often along nerve-trunks, or is indefinite in its distribution. It is usually most marked in the paralyzed parts. There is

occasionally tenderness over the nerve-trunks. Pain and tenderness are at times marked enough to cause the paralysis to be entirely overlooked and a diagnosis of rheumatism or scurvy to be made. The extremities are often held rigidly and all motions as vigorously resisted as possible because of the pain on motion. This combination of rigidity and resistance is possible, of course, only when the muscles are but partially paralyzed or when some of them are intact. The failure to appreciate the significance of this condition of combined flaccidity and spasticity has led, in my experience, to many errors in diagnosis during the acute stage. In one of my own cases it was necessary, on account of the rigidity of the leg and the pain which attempted motion caused, to give ether enough to dull sensation before it could be determined whether the trouble was an infantile paralysis or a disease of the hip joint. When pain was no longer felt the affected extremity was flaccid while the muscular tone was normal in the rest of the body.

ABORTIVE TYPE

There is no doubt that the disease occurs very frequently without the development of any paralysis. The term "abortive" ought strictly, of course, to be limited to the cases in which there is no paralysis. There is, however, another class of cases, in which the paralysis is very slight and lasts but a few hours or days, which is on the border-line between the abortive type and the ordinary spinal type. These cases are very easily overlooked clinically unless the symptoms are very carefully studied.

DIAGNOSIS

The diagnosis of infantile paralysis of the spinal type after the development of the paralysis is, of course, very easy. The great difficulty at present lies in making the diagnosis before the appearance of the paralysis. Sweating, marked nervous irritability and hyperesthesia are present in many instances before the onset of the paralysis, but they are not at all constant. If they are present, they are strong evidence in favor of infantile paralysis, but their absence does not count against it. Hyperesthesia is the most constant and the most important symptom of the three.

Although leukopenia occurs in animals during the early part of the acute stage of infantile paralysis, it is certainly not a constant symptom in man and in many instances is replaced by a hyperleukocytosis. Further experience is necessary to determine of how much value the leukocyte count is in the early diagnosis of infantile paralysis. At present it is

of little or no assistance. While it is possible that there is a lymphocytosis in the early stages of infantile paralysis, there is at present not sufficient evidence to show whether either a relative or an absolute lymphocytosis is at all a constant phenomenon. If further investigation shows that it is, it should be of considerable assistance in the early diagnosis.

Experimentally, there is an increase in the number of cells in the cerebrospinal fluid during the prodromal stage before the appearance of the paralysis. The polynuclear cells at this time exceed the mononuclear. After the appearance of the paralysis the mononuclear cells quickly outnumber the polynuclear. A fibrin clot is often formed in the prodromal or early part of the acute stage. Frissell, in the only instance in which lumbar puncture has been done in man during the preparalytic stage, obtained a slightly opalescent fluid which gave a marked protein reaction with Noguchi's test and showed an excess of polynuclear cells. The formula had begun to change to the lymphocytic, however, before the paralysis developed. Lumbar puncture ought, therefore, to provide a most valuable means of diagnosis in this disease during the preparalytic stage. Its value is considerably limited, however, by the fact that there is nothing whatever characteristic about the early symptoms of infantile paralysis, and, therefore, nothing to definitely suggest its use. In order to recognize the disease early, therefore, before the onset of the paralysis, it would be necessary to do a lumbar puncture on every sick child, which hardly seems a rational procedure.

During the acute stage of infantile paralysis the cerebrospinal fluid is clear, not infrequently under somewhat increased pressure, often forms a fibrin clot on standing, and always contains an excess of cells. These are chiefly of the mononuclear type, most of them being lymphocytes. These changes are, however, identical with those found in tuberculous meningitis, the disease with which it is most likely to be confounded. An increased protein content is also found by the Noguchi test in both diseases. A positive diagnosis between them can only be made, therefore, by the examination of the cerebrospinal fluid for tubercle bacilli. These can be found in the great majority of the cases of tuberculous meningitis if the examination is careful enough. They are more than likely to be missed, however, in the ordinary routine examination. The characteristics of the cerebrospinal fluid in infantile paralysis are, of course, so different from those in meningococcal, influenzal and pneumococcal meningitis that no confusion with these conditions is possible.

The only possible method of making the diagnosis of infantile paralysis of the spinal form before the onset of the paralysis is, therefore, by lumbar puncture. In order to be of much assistance, however, this must be done very generally in sick children during the summer months, because there is nothing characteristic and usually nothing even suggestive about the early symptoms.

70 Bay State Road.

THE CONTROL OF EPIDEMIC POLIOMYELITIS*

SIMON FLEXNER, M.D.
NEW YORK

Epidemic poliomyelitis has, since its appearance in 1907-08 along the Atlantic seaboard, extended over the entire United States. This wide distribution has fortunately not been attended by a regular and uniform prevalence of the disease in all communities. Indeed, considerable territories would seem to have escaped its ravages, although few, if any, of the states have remained entirely free from invasion. The number of persons attacked can be only conjectured, but it is probable that it reaches into the thousands. The mortality has been the average noted in the European epidemics, and has approached 10 per cent. Undoubtedly the mild or abortive forms of the disease have prevailed along with the severer paralytic types, and in many instances their nature has been certainly overlooked. Among the paralytic cases all grades of the affection have been encountered, and the number of cases in which complete recovery without residual paralysis has taken place would appear to have been not inconsiderable. In other words, the American epidemic of poliomyelitis is in agreement with the earlier European epidemics in all essential respects, and differs from them only by reason of its wide distribution and great total number of cases. This variation is to be explained probably not by supposing that the conditions for the prevalence of the disease in the United States were more favorable than in Europe, but because of the greater extent of territory embraced under one government. Possibly also the United States have suffered disproportionately and more severely than European countries because of the failure, in many communities, to make prompt recognition of the nature of the malady, and because of the want of a body of authoritative sanitary regulations that could be put into rapid operation in the effort to delimit the spread of the disease through the employment of methods of quarantine. I am convinced that the disease in some communities was mistaken for periods of many months for epidemic meningitis, a fact not highly surprising in view of the lack of general knowledge regarding epidemic poliomyelitis

*From the Laboratories of the Rockefeller Institute for Medical Research.
*Based on remarks made before the Association of American Physicians at Atlantic City, May 9, and the American Pediatric Society at Lake Mohonk, New York, June 1, 1911.

that existed throughout the country, and in view of the common occurrence of marked symptoms referable to meningeal irritation in the course of the malady.

The question of the control of epidemic poliomyelitis is one of high interest at the present time. This control may be of two kinds, namely, that effected through the employment of measures of prevention, and that through the employment of modes of treatment. Of the two possible means of control, the first, that through prevention, is to be given the place of prime importance, for it is not only more humane and scientific to prevent a disease rather than to effect its cure, but in the present instance the knowledge available makes prevention a possible achievement, while there exists no known means of therapeutic control worthy the name.

The measures of prevention employed should be those based on knowledge of the mode of infection that clinical observation and experimental investigation have thus far supplied. At any given period we can apply intelligently and with confidence only those preventive measures that are founded on such knowledge. It would seem to be established that the human agency of transfer of the infectious agent does occur and perhaps frequently. Moreover, this human agency includes not only the actively infected or ill, but also healthy persons who perform the part of intermediaries between the stricken and the well who are to develop the disease. To express this point in somewhat more technical language, we must accept for the present the existence of both active and passive carriers of the infectious agent of epidemic poliomyelitis and accord to each a share in the distribution of the agent through the implantation on other susceptible persons. Hence, in the effort to control this distribution, there should be employed adequate measures of isolation and quarantine of the sick as well as those in immediate attendance on the sick.

We are not sufficiently accurately informed of the period of survival of the infectious agent within the active and passive carriers to enable us to state precisely what the period of quarantine should be. We possess some data, not, however, overaccurate and convincing, based on the period of development of secondary cases of the disease, that suggest that the virus may persist in the infected in an active state for several weeks, and we further possess experimental evidence to the effect that in inoculated monkeys the virus may survive in the mucosa of the nasopharynx at least for several weeks and even several months (Osgood and Lucas, Flexner and Clark). This long period of survival in the monkey would,

however, appear to be exceptional. In many instances the virus cannot be discovered in the mucosa as early as one, two or three weeks after the appearance of the paralysis (Flexner and Clark). I am disposed, therefore, to view the examples of long persistence of the active virus in the monkey, with which, doubtless, corresponding examples among human beings will be found, as the equivalent of the chronic carriers of bacteria among men and animals in other well-established types of infectious diseases. Such chronic carriers constitute not only and fortunately an exceptional class, but in framing our practical measures of prevention we have considered them, up to the present time, in rather an incidental way. Thus, for the present it would seem that a period of isolation of from three to four weeks would be sufficient in ordinary cases of epidemic poliomyelitis, it being understood that when the acute or febrile course of a case of the disease is prolonged, the period of isolation be lengthened accordingly.

The efficiency of any group of preventive measures will depend on the directness with which they deal with the source of the infectious agent that they seek to restrain. We have progressed very far into the management of an infectious disease when we have learned the portals of egress and of ingress of the infectious agent. Such knowledge of this kind as we possess regarding epidemic poliomyelitis is based wholly on animal experiments, and hence the degree of its application to human beings has still to be established.[1] It has been shown that in the monkey the virus of poliomyelitis passes from the central nervous system into the nasal mucosa, and it has been found that monkeys can be infected more readily by applying the virus to the nasal mucosa than by any other means except direct intracerebral inoculation. It is for this reason that I believe special attention should be accorded the nasal and buccal secretions of persons affected with epidemic poliomyelitis during the period of isolation, and even for a period afterward. The facts known concerning the relation of the nasal mucosa to the virus of poliomyelitis must be taken at precisely their true value, and must not be considered to exclude other modes of infection by way of other channels in human beings. Hence beside the attention given to the destruction of the nasal and buccal secretions, and to the keeping clean and free from these secretions the hands and other

1. Since this was written Landsteiner, Levaditi and Pastia (Semaine Medicale, 1911, No. 25, p. 296) have established the presence of the virus of poliomyelitis in the tonsils and pharyngeal mucosa of a child who succumbed to infantile paralysis during the acute stage of the disease.

parts of the body as well as the clothing, vigilance should not thereby be relaxed in dealing with all the secretions in a sanitary manner.

Studies of the manner of travel of and the route taken by the disease in thinly populated districts especially have failed in not a few instances in supporting fully the idea of the human agency in the transmission of the infection. Studies of this kind cannot be made satisfactorily in cities or even in towns for the reason that the contact with persons is too frequent and promiscuous to permit of accurate tracing. Owing to this discrepancy, some other agencies have been invoked to account for the transmission of the infection over wide areas, and the chief ones of this character have been domestic animals and insects. Paralytic diseases among domestic animals are known and not highly infrequent. They have been noted among dogs, horses and fowl, but thus far it has not been found possible to correlate the paralytic diseases of the lower animals and those of man. Perhaps the most frequently observed coincidental paralytic diseases have been between hens and human beings. Undoubtedly since the wide prevalence of epidemic poliomyelitis, the existence of a paralytic disease among barnyard fowl has been more commonly noted. Possibly the condition has not actually become more frequent, but owing to the circumstance mentioned it has been oftener observed. It would appear that the paralysis among fowl is caused not by lesions of the central nervous system, but by lesions of the peripheral nerves and that it is due to a peripheral neuritis. It has not been found possible to transmit by direct inoculation the paralytic disease from chicken to chicken, or from chicken to monkey, or from paralytic monkey to chicken (Flexner and Lewis). However, it has been found possible to develop the paralysis in the laboratory by keeping the chickens in confinement for some time, and by supplying them an unusual and doubtless improper form of food (Flexner and Clark). It has proved as little possible to transfer the paralytic affection of dogs from one individual to another by direct inoculation or from dog to monkey or from paralyzed monkey to dog (Flexner and Lewis). These failures do not, of course, exclude the possibility that a reservoir for the virus may exist among domesticated animals that do not even respond to its presence by developing paralysis or other conditions which could be recognized as resembling poliomyelitis in man. The manner of the action of the virus of poliomyelitis in rabbits provides an illustration which shows how necessary it is to avoid general deductions in this field. At first it was strenuously denied that rabbits could be infected at all with the virus of poliomyelitis, and the examples of sup-

posed successful inoculation reported were entirely disbelieved (Krause and Meinicke, Lentz and Huntemüller); but it must now be accepted that young rabbits occasionally, but by no means generally, are subject to inoculation with the virus of poliomyelitis, at least after it has passed through a long series of monkeys (Marks). Apparently a small percentage only of the inoculated rabbits develop any obvious symptoms, and these die, as a rule, during convulsive seizures which come on suddenly. A given virus has up to the present been sent through a series of six rabbits, after which it has failed to be further propagated. From the sixth series it has been reimplanted on the monkey, in which animal typical paralysis has been produced (Marks). It remains to add that the rabbits which succumb to the inoculation do not show any characteristic lesion of the central nervous system or other organs, as far as has been determined. The monkey, on the other hand, invariably shows the typical lesions of the central nervous system.

Insect contamination with the virus would serve, were it proved not only to be an experimental possibility but to occur in nature, to clear away any present apparent discrepancies in the epidemiology of the disease. In this connection it should be stated that not only does epidemic poliomyelitis spread over a wide territory, but its spread is not promiscuous, but along the routes of human travel. Therefore insects that seek human habitations and routes of travel, that possess the power to migrate over a considerable territory, that affect all classes of society, that abound during the period of greatest prevalence of the disease, and that do not wholly disappear at any season, should be the first to come under suspicion. Many, if not all, of these conditions are fulfilled by the common house fly.

Laboratory-bred flies have been subjected to contamination experiments with the virus of poliomyelitis, from which it appears that they are capable of harboring the virus on their bodies in a living and infectious state for at least forty-eight hours. Moreover, it has developed that the virus also survives within the viscera of the insects for some time. (Flexner and Clark.) It should now be readily possible to secure flies from rooms in which cases of acute poliomyelitis are, in order to ascertain whether in nature they also become contaminated with the virus of the disease.

When we turn to the question of the control of poliomyelitis by the cure of the disease we refer of course to the reduction in the mortality and in the crippling effects which it causes. In respect to this question

we find ourselves provided with scant knowledge that at the moment is capable of being applied practically. Experimental studies have shown clearly that recovery from the disease is effected by means of immunity principles that appear and persist for a long time—perhaps for years—within the blood. It has indeed been found possible in animals to apply the blood serum taken from recovered human beings and monkeys in such a way as to prevent the development of paralysis in monkeys following the inoculation of the virus (Flexner and Lewis). More recently still the fact has been ascertained that several larger domestic animals, including the horse, sheep, goat and pig, can be made to develop the immunity principles in their blood by subjecting them to injections of the spinal cord and brain of monkeys containing the living virus (Flexner and Clark). But these sera do not hold out any great hope of beneficial application in the treatment of developed poliomyelitis in human beings, for the reason that they are relatively weak in the immunity principles. An effort is therefore being made to approach the therapeutic problem through another avenue, namely, the employment of drugs. At the outset it is patent that since the drugs must come to act in the region of the central nervous system, the choice is restricted to those that beside possessing antiseptic properties can yet be applied to that sensitive part. We possess almost no drugs that exhibit the property of "internal antisepsis" so called, or in other words, are capable of exerting their antiseptic action in the interior of the body, in the presence of the proteins of the blood and tissues. Just here account should be taken of the pathogenesis of epidemic meningitis, since it is on it that the selection of the drug and the manner of its administration may come to be based. The evidence at hand points to the meninges as being the location of the primary lesion of the disease. It would seem as though the virus of poliomyelitis became first implanted on the leptomeninges, in which it developed, causing a cellular exudation that affects especially the blood-vessels, the partial obstruction of which leads to the secondary production of the lesions of the nervous tissue itself. It is indeed not excluded that a direct action of the virus of poliomyelitis on the ganglion cells takes place, but this effect, if produced, appears to be less general and constant than the effects on the meninges. Hence the problem that presents itself is one that has to do with the control of the primary meningeal lesions, that in turn are caused by the virus present within the interstices of their tissues, as well as doubtless, at some stage of the process, within the cerebrospinal fluid itself. What is required then are antiseptic drugs having a special power

to destroy this virus, and of very low toxicity, that can be made to exert their principal action on the meninges and in the subdural space. We possess in hexamethylenamin (urotropin) a drug which fulfils certain of these conditions. It is an internal antiseptic of some power, and is eliminated in some degree from the general circulation into the subdural space (Cushing and Crowe). On empirical grounds the drug has already been administered in cases of epidemic poliomyelitis, but whether with any definite effect is not known. Administered to monkeys prior to or coincident with inoculation and repeated daily afterward, hexamethylenamin is capable in some instances of preventing paralysis, and in others of lengthening materially the incubation period of the disease (Flexner and Clark). However, its powers in this direction are limited. On the other hand, its chemical composition is such as to permit of the addition of other chemical groups to the original molecule, in virtue of which the antiseptic power may be intensified. Through the employment of this means, a number of relatively non-toxic compounds have already been produced, which far exceed in internal antiseptic value the original drug, and some of these have already been applied experimentally with some degree of success to the prevention of the development of the paralysis following inoculation of the virus (Flexner, Jacobs and Clark). Whether any of these drugs will prove applicable to the treatment of human beings the victims of poliomyelitis it would be hazardous to predict, but it seems not improbable that some advance should be made along this line of investigation.

The case for the treatment of human beings is less hopeless, as I view it, than is commonly believed. It should be taken into account that much of the supposed damage inflicted on the nervous system of human beings at the onset of the paralysis is remediable. For the brunt of the disease falls not on the nervous tissue, but on the meninges, where it can in turn be opposed by therapeutic measures; and the severer nervous lesions are not in the most instances absolute, but they are merely relative and often probably merely functional in nature, since as many as 25 per cent. of the paralyzed may make complete recovery, and there is restored to a far larger percentage, by the usual processes of delayed resolution, a considerable degree of power in and use of muscles once severely paralyzed.

INFANTILE PARALYSIS

THE MOST PROMISING OUTLOOK FOR IMPROVEMENT IN TREATMENT FROM THE STANDPOINT OF THE PEDIATRICIAN

J. H. M. KNOX, JR., M.D.
BALTIMORE

GENERAL STATEMENTS

We now know that epidemic infantile paralysis is a result of an infective process produced by a specific virus which affects particularly the vessels of the meninges, leading to marked hyperemia, infiltration and inflammation, and to secondary involvement and degeneration of certain of the adjacent nerve-cells and fibers. The disease itself is a self-limited one, terminated by the production within the organism of antibodies to the specific virus. The duration of the acute symptoms may vary from several days to as many weeks, when they may end fatally or in complete recovery, or may be followed by the palsy of one or more muscles, dependent on the site and the extent of the nerve affection. The early paralysis is always of greater extent than the residual palsy, and is due apparently to pressure on nerve trunks by the edema and infiltration of the meninges. It is only after the disappearance of these acute phenomena that the extent of the lasting palsy due to nerve degeneration can be ascertained.

The *treatment* of the disease as presented to the pediatrician consists in the first place, (*a*) in an attempt to lessen the severity of the attack, (*b*) in an effort to render the patient more comfortable during the course of symptoms, and (*c*) in the prevention of deformities, the result of disturbed muscular balance; and secondly, in averting the spread of the disease from the patient to others.

DIAGNOSIS

In regard to the effort to alter the course of the disease there are at present great difficulties. The diagnosis of the malady can rarely be made from the symptoms until the development of the paralysis. It usually begins with a febrile onset accompanied frequently with sore throat or digestive disturbances and more or less general hyperesthesia and sweating. These are rarely sufficient to distinguish it from other

infectious ailments. However, in an epidemic the occurrence of these symptoms in a patient should lead certainly to the suspicion of poliomyelitis. The diagnosis can be considerably strengthened by an examination of the spinal fluid. Here there is an increase in the number of cellular elements, particularly in the lymphocytes and in the protein contents of the fluid. The value of this aid in diagnosis was strikingly illustrated in a case reported by Dr. Frissell,[1] in which the symptoms of infection were present but physical examination otherwise negative. The condition of the spinal fluid sent to Dr. Flexner was found to resemble that seen in monkeys inoculated with the virus of the poliomyelitis, just before the onset of paralysis. By the same means the presence of meningitis, often difficult to distinguish clinically from certain forms of infantile palsy, can usually be excluded.

The laboratory may also be of assistance in the diagnosis of the disease by testing the sera of the suspected patient on monkeys; if the condition is poliomyelitis the blood-serum of the patient mixed with an active virus *in vitro* will neutralize it and the effect of the mixture when injected into a susceptible animal will be *nil*.[2] This method would be particularly serviceable in the recognition of sporadic and unusual cases in their early stages.

The disease, then, being recognized or suspected, have we any means at hand to control its course? Certainly none that is specific or satisfactory. Active immunization by intracranial injections of the virus has been repeatedly carried out with success in susceptible monkeys,[2] but a sufficiently active curative serum to be of therapeutic value for human beings has not yet been obtained, although serum from immunized animals or from those recovered from the disease will protect a susceptible monkey when injected intraspinally twenty-four hours after the injection of the virus. More hopeful as a therapeutic agent is the administration of hexamethylenamin (urotropin). Cushing, Crowe, Morris and others have shown that after the administration of this drug formaldehyd quickly appears in the blood and secretions of the body, including the spinal fluid, and it is thought that this antiseptic may destroy the virus, or at least deter its action in the congested meningeal vessels and on the nerve-cells.

On the ultimate result of treatment with this drug and with closely related products it is too early to speak positively from clinical experi-

1. Jour. Am. Med. Assn., 1911, lvi, 661.
2. Jour. Am. Med. Assn., 1910, lv, 1105.

ence. The number of cases in which good results are reported from the use of hexamethylenamin in small doses by the mouth is constantly growing and there is considerable experimental evidence in its favor.[3]

Thus it was found at the Rockefeller Institute, when the active virus was injected intracerebrally into monkeys, to which hexamethylenamin had been given for some time, in a proportion of these animals the incubation period of the disease was prolonged and in some the paralysis was entirely prevented. The effect of hexamethylenamin is probably not lasting and it gives no increased resistance to reinfection at a later period. It does, however, hold out some hope that if given before the paralysis begins this may be diminished, and it may be serviceable also in preventing the escape of the virus from the body.

TREATMENT

The duty of the physician to his patient is by no means completed in his rather unsatisfactory attempt to make a diagnosis and to lessen the severity of the malady. He can do much to make the child more comfortable. He is dealing with an infectious disease and one associated usually with more or less discomfort and pain. Complete *rest* is the first and most essential factor in the treatment of the disease. This must be secured, with an abundance of fresh air, preferably in the open.

The patient should be kept perfectly quiet and, better, completely isolated. The bowels should be opened and moved regularly and the diet should be light and nutritious as in other febrile conditions.

The suggestion of Lange[4] and Hohman[5] that the spinal column should be immobilized in a plaster cast will probably be serviceable in those cases in which the pain is particularly severe. Occasionally sedatives, best codein or morphin, may be necessary.

Cupping near the spinal column by the Bier method has many advocates, but it is doubtful whether intraspinal congestion can be relieved by this method.

A warm bath or pack with a cool application to the head may have a quieting effect in the early stages. The administration of nerve tonics, especially of strychnin, and of irritating procedures, such as electrical treatment or massage, must be carefully avoided at this time.

When the acute symptoms have subsided the patient enters the second stage of the illness, in which, although the fever has gone, there may be

3. Jour. Am. Med. Assn., 1910, lv, 1804.
4. Tr. Am. Pediat. Soc., 1910, xxii, 170.
5. München. med. Wchnschr., 1909, lvi, 2508.

sensitiveness along the nerve trunks and on passive motion; there may be also contraction of the limbs due to pain which does not allow them to be brought into their normal positions. It is important that the absolute rest should be continued and that any over-stretching of paralyzed muscles, either from pressure of bed clothes or from gravity or from the pull of sound muscles, should be prevented by the arrangement of sand bags, pillows, etc. At this time, heat as a moist or dry pack may relieve the tenderness.

The patient may be said to enter on the convalescent stage of the disease when the sensitiveness has disappeared and there are no contractions due to irritation. This stage lasts, as pointed out in the admirable report on infantile paralysis in Massachusetts in 1909, until all potential power has been regained and until the deformities require no further attention. It is important to emphasize the fact, not sufficiently understood by the physician, that the muscle power returns continuously, though slowly, through months and even years, and during all this period repeated observations and treatment are indicated.

It should be the special endeavor at this time to prevent deformity and assist in the recovery of nerve and muscle power. The normal balance of the muscles about the joints should be maintained at all hazards, and the over-stretching of paralyzed muscles by the contraction of unaffected opposing muscles should be prevented. Judson[6] has emphasized the value of keeping the patient long in a recumbent position. He feels that the large predominance of the residual paralysis in the lower as compared to the upper extremity is due in part to the attempt of the patient to sustain his weight on the impaired muscles in the legs and feet. No corresponding exertion is demanded of the arms and hands. He suggests in many cases to extend the recumbent position as long as eighteen months.

The means at hand for stimulation of nerve and muscles are electricity, faradic when possible, and when response to this is lost, a galvanic current should be used; applications of various forms of heat, for the improvement of the circulation and the prevention of the comparatively low temperature of the paralyzed muscles, and massage, which improves the circulation and supplies artificial stimulus to both nerves and muscles. All these measures, however, are claimed by Sachs[7] and Strunsky[8] and others to be of much less value than what may be called

6. Denver Med. Times, Oct. 1, 1907.
7. Jour. Am. Med. Assn., 1910, lv, 48.
8. Am. Jour. Dis. Child., 1911, i, 266.

muscle training. Strunsky in a recent article insists that the dominant element of success in the restoration of function is in *suggestion,* in securing the *cooperation* of the patient in the effort to make the desired movement, and that massage, passive motion and electricity, when helpful, are so because they are means of obtaining this end. "A bright child," he says, "one susceptible to impressions, makes better progress during the treatment than the stupid child." "Well directed massage may be the instrument that arouses the will power to concentrate to the utmost during muscular contraction, and leads to the building up of the mental and motor brain cells." An interesting contribution to this subject might be made on paralyzed monkeys and a comparison instituted between the prevention of atrophy or the restoration of function to muscles treated by electricity, by massage or by having such animals attempt voluntarily to make certain special movements. Microscopic examinations of such material might be instructive.

The surgical treatment of deformities resulting from infantile paralysis such as muscle and tendon transplantation and nerve grafting, or a discussion of the many effective mechanical devices for preventing and correcting deformities, does not fall within the scope of this paper. It remains only to refer briefly to the prevention of the spread of the disease from the patient to others.

Mention has already been made of the probable value of hexamethylenamin or similar germicidal drugs. It may be that the administration of this drug to those in attendance on a patient suffering from infantile paralysis may diminish their susceptibility to the disease. It should certainly be given to the patient during the acute stages, not merely for its possible effects on his infection, but because by this means the danger to those exposed may be lessened.

The studies at the Rockefeller Institute have shown that at least one portal of entry of the virus is in the nasopharynx and that the virulence of the virus is destroyed by the application of 1 per cent. hydrogen peroxid. It is rational, therefore, to apply this disinfectant to the nasopharynx of both patient and attendant at frequent intervals, and as Osgood and Lucas[9] have shown that the virus may persist for at least five months or longer in the nasopharynx of monkeys, this treatment of the patient should be continued, at perhaps longer intervals, for a more or less indefinite period.

804 Cathedral Street.

9. Jour. Am. Med. Assn., 1911, lvi, 495.

REPORT OF SPECIAL COMMITTEE ON ANTERIOR POLIOMYELITIS

To the President and Members of the American Orthopedic Association and of the American Pediatric Society.

The Joint Committee appointed by your Societies in May, 1910, to communicate to State Boards of Health and other health authorities with regard to anterior poliomyelitis, would respectfully report as follows:

After the organization of the committee, circulars were sent to the medical journals and letters to the health commissioners of each state and to each provincial health officer of Canada. These letters urged the physicians and health authorities to study and quarantine the disease, and the journals gave publicity to most of these circulars. The letters to the health officers requested them to take notice of the serious character of the epidemics, the spread of the disease and its contagious nature, and asked them to make the disease reportable and to undertake a field study of epidemics. This work was undertaken by Dr. Snow, who served as secretary of the committee.

It is an interesting fact that at this time anterior poliomyelitis has been made a reportable disease in 23 states, is not reportable in 21, and no information can be obtained from the others. It is reportable in Ontario and British Columbia, but not in the other provinces as far as known.

The committee is of the opinion that with the enormous spread of the disease in the United States in 1910 it is advisable to continue the campaign instituted a year ago, and to send a circular of information and warning to public health authorities and to the medical press.

Following is the circular issued by the American Orthopedic Association and the American Pediatric Society, in reference to acute epidemic poliomyelitis, and addressed to health authorities and boards of health.

Anterior poliomyelitis is, so far as known, a communicable disease, being communicated from one patient to another and also by means of a third person. It occurs in epidemics and tends to spread along the lines of greatest travel. There is reason to believe that it is prevented from spreading by quarantine, and with the great prevalence of the disease in the summer of 1910, it is the opinion of this committee that it is essential that it should be made a reportable disease in all states in order that its presence may be detected and its spread guarded against.

Of particular significance are the so-called abortive cases, where indefinite ailments occur in children in communities where frank paralysis also exists. These abortive cases of this disease are undoubtedly a source of infection, and their record and study is of much importance. In a community where cases of anterior poliomyelitis occur cases of illness with sudden onset of fever and meningeal symptoms should be closely watched and regarded as possibly infectious. In such cases even recovery without paralysis does not establish the fact that the case was not abortive anterior poliomyelitis.

All cases of the disease should be strictly quarantined, sputum, urine and feces being disinfected, and the same rigid precautions being adopted as in scarlet fever. This quarantine should, in the opinion of the committee, last four weeks in the absence of definite knowledge as to when the infection ends. Chil-

dren from infected families should not be permitted to go to school until the quarantine is abandoned. The transportation or transfer of acute cases in public conveyances should be strictly forbidden. It would be very desirable to adopt provisional quarantine measures in suspicious cases in a community where an epidemic prevails. The report of all cases of poliomyelitis to the public health authorities should be enforced by law, and all deaths from this cause should be properly described and registered. A careful study of epidemics by public health authorities is strongly advised.

ROBERT W. LOVETT, Chairman.
HENRY KOPLIK.
H. WINNETT ORR.
April 28, 1911. IRVING M. SNOW, Secretary.

DISCUSSION OF SYMPOSIUM ON POLIOMYELITIS.

DR. ADAMS: The question of the prevention of epidemics, or recurrence of epidemics, is of course, the burning subject of the day. The curative measures are so much in doubt that we must rely upon prevention. With this idea in view I addressed a letter to every children's hospital in the country last fall asking a certain number of questions, my object being partly to allay the anxiety which had sprung up in the District, particularly with the Boards of the Children's Hospital, as to the spread of the disease. There had been some criticism of the staff for accepting cases of the disease during the summer months. There were about thirty cases admitted during the summer which were all considered as being beyond the period of infection; that is, more than three weeks old. After the return of my colleague, Dr. Acker, and myself, two infants were sent to the hospital, admitted by the resident, and this acted among the ladies of the Board as a firebrand to such an extent that open and secret criticism of the staff and management of the hospital was indulged in and the president of the board was appealed to. The methods taken for the prevention and care in other institutions was cited as evidence of lack of care exercised in this institution. The president sent for me and I explained the case and then put it before the board of directors and they instructed me to go before the lady board and try to allay their anxiety. This was the principal reason for addressing this letter to the institutions. I confess that I was comewhat surprised at the answers received from these hospitals. Among the inquiries were: Do you admit to the wards cases of poliomeylitis? Do you consider the disease contagious, and in what stage? Have you ever had a case of poliomyelitis originate in the hospital, or have you any evidence that the disease has spread from patients admitted to the hospital? Do you isolate patients and to what extent? Some have not as yet isolated the cases, but intended to do so. One well-known institution had the patients in an adjoining room and the nurses and doctors were required to put on gowns or special garments on entering the room. Another institution had a little more complete isolation, and one very large institution in New York reported that it did not take any means whatever to isolate and did not consider the disease a contagious one. As to the disease originating in the hospital, the invariable reply was, no. That was our experience in the hospital.

Now, I believe, of course, that these institutions will very shortly practice isolation, particularly will this be so if the city requires compulsory reporting of cases. In the District of Columbia an investigation has shown about 500 cases reported, but I know that is far from the number of cases that actually occurred, for I know of one personal friend who did not report a single case although he had quite a number. I have heard others express themselves as not

having reported them. It must be taken into consideration, too, that these cases occurred at a season of the year when Washington's population is greatly decreased. The population decreases there very rapidly with the beginning of June, when every one who is able to get out of the city does so. That would indicate that the disease prevailed to a considerable extent there. Now I am supporting the Public Health and Marine-Hospital Service in their efforts for compulsory isolation, and think this should be strictly enforced. The health department should take up this question and not leave it to the conscience of individual physicians. I am sorry to express myself in a way that might reflect on the conscience of the physicians of the day, and yet many who are otherwise conscientious are absolutely indifferent to the methods of prevention and positively refuse to use any means of prevention of this veritable scourge which has increased its virulence so recently in this country.

DR. WESTCOTT: In reference to the treatment of one of the most distressing symptoms of the disease, pain or hyperesthesia of the joints, I would mention the result of a lumbar puncture which I made in the case of a daughter of a professional friend last winter. The case was a severe one. The involvement of the body was quite general, but the most distressing symptom was the pain in the knees. Morphin was given in considerable doses, but succeeded only in relieving the pain for an hour or two, when it would return as severely as before. At the suggestion of Dr. Spiller of Philadelphia, I made a lumbar puncture and withdrew more than 15 c.c. of spinal fluid under considerable pressure. The relief of the pain was almost instantaneous; in fact, before I left the house the child was comfortable and there was no complaint of pain afterward.

DR. CHAPIN: There is one aspect of this disease of considerable interest. Years ago we never thought of contagion with reference to it, but in recent years the epidemic type has come on. I think it would be very instructive if some of the men here who have a large clinical experience could tell us their opinion as to its contagiousness.

DR. JACOBI: It may be of some interest to the members to know how the disease looked fifty or more years ago. My first knowledge of the disease was acquired from an article by von Heine, who, I think, was the first man who wrote extensively on the subject. The disease at that time was called infantile paralysis. It was also called by the misnomer of dental paralysis, as all sorts of diseases were at that time attributed to the process of dentition. That name has, of course, disappeared. Heine wrote an extensive article on this disease in 1840. Then he wrote a book on this subject in 1860, and a second edition in 1869. He described the symptoms which are noted to-day. He has quite a number of cases in which he describes the brain symptoms accurately, but he never made an autopsy. Even at the time of the second edition he had not seen an autopsy of the brain or spinal cord of such a patient.

My own experience began in 1854-55. I mentioned the subject in an antediluvian book of mine which appeared in 1862, and which I mention only because it is out of print. In that book I referred to infantile paralysis, the cases of which were a little different from those we now see. What I knew was that a child perfectly well up to the time he was put to bed in the evening was found to be paralyzed in the morning; no fever, but paralysis; not always paraplegia. There are very few cases of paralysis of all four extremities. There would be rapid improvement in four or five days, and then very slight improvement for five or six weeks and then absolute standing still after that time, with remaining paralysis in some of the muscles. When there was paraplegia there generally remained paralysis of one limb. At that time I never saw paralysis of a

sphincter. There were other cases in which the child had a pneumonia or scarlet fever, with high fever; was not taken up for a number of days and then when first taken out of bed found to be paralyzed. These were the only cases, I believe, I saw at that time that commenced with fever, the fever being explained by the other disease. No one knew the cause at that time. It looked to me as if the only explanation was a sudden hemorrhage, perhaps in the lumbar region or cervical region, to explain the paralysis. That was what I believed I knew at that time. They recovered, I believed, through absorption of the hemorrhage. But there never was a perfect recovery.

What I did was as follows: I applied ice; now and then used mustard plaster and tincture of iodin, gave a purgative, calomel or saline; gave ergot in the beginning, but never strychnin at first. I never used electricity in the beginning. I used galvanism later on. It takes a great deal of patience to do anything with electricity, as you all know. An assistant of mine at that time took the trouble, in a child that was paralyzed and atrophied, to employ electricity. It took him two years of daily application of the current. He certainly improved that absolutely paralyzed child a great deal. So, in such cases even now it may be relied on to a certain extent if there is any one who has sufficient patience to use it. I have found that now and then in older cases strychnin would do good, but never when given internally; it should be given subcutaneously.

DR. COTTON: The first case of infantile paralysis I ever diagnosed in the incipient stage was one about twenty years ago. While returning to my clinic a woman I knew met me and begged me to run in and see her child, who she said was well the evening before, playing on the back porch in the gathering twilight of a November evening, but who that night had had fever and she wanted me to see him. In examining the little fellow, 4 years old, I discovered that he could not draw his right hand away and then that he could not lift the lower extremity, but with the left hand he pushed me away. I returned to the college and took over several students with me to see a case of infantile paralysis.

In 1893 a parent came into my clinic with a child having monoplegia, with a note from an old doctor in Iowa. It was a typical case, and was so presented to the clinic. I sent a note of thanks to the doctor and was surprised when two weeks later he sent me another case and a letter saying that he believed it must be epidemic, as he had had seven cases in his limited country ride. Now it occurred to me while reviewing the history of this disease, how many of these little local epidemics may have occurred without ever having been reported before the attention of the profession was focussed on this disease.

Since seeing my first case twenty years ago, I have seen five cases in the incipiency. From the recent explanation of the pathology of the disease, recognizing that it is an inflammatory process, that much of the early paralysis is due to pressure, congestion, inflammation and edema, it occurs to me that a rational treatment is one of depletion. Elimination of the unknown toxin is certainly desirable; profuse catharsis, diaphoresis, diuresis, depletion, and rest. And by blood-letting, too, it seems to me good may be accomplished, by leeches, natural or artificial. This would be good also for the counter-irritant effect.

About the time I received my medical degree, Brown-Séquard's application of ergot and bromid to diminish hyperemia of the spinal cord was attracting attention. It impressed me very much, and from that time to this I have never diagnosed spinal hyperemia without thinking of that application of bromid and ergot, and I have always employed it. It seems to me it is indicated in these conditions. I would also use atropin. In the last eighteen months I have seen three cases which I have treated in this way.

DR. BLACKADER: I would like to ask one question. In the epidemic in Montreal I did lumbar puncture in several cases with great relief and I would be glad to know just how far Dr. Flexner would consider that procedure of value in this disease. As to the relief of pain, I had several cases which would verify Dr. Westcott's observation as to its value. It seems to me there was some relief also of the other symptoms.

DR. CHURCHILL: I would like to ask Dr. Lovett if he knows of any explanation for the large number of cases in Minnesota. Was there any epidemic in Sweden in 1910? Of course, it is not far from Minnesota to Sweden nowadays, and I wondered if there was any connection between that and the immigration.

DR. CRANDALL: Dr. Morse had expressed surprise that certain earlier writers did not lay stress on pain as a symptom of poliomyelitis. I saw my first cases twenty-three years ago, when several patients came to the Polyclinic during the early fall. They were very similar to those described by Dr. Jacobi. There was little or no pain, but paralysis was the most prominent symptom. The child would be put to bed well and in the morning would wake paralyzed. It is well recognized that the clinical type of the disease is somewhat variable. It seems certain that the most common clinical type three or four decades ago was rather different from that of to-day. Having formed my conception of the disease on these earlier cases, I found it necessary a few years ago to readjust that conception, because of a different prevailing type. This variability no doubt explains the varying clinical pictures that have been drawn at different periods.

DR. MORSE: As I understand the pathology of the disease, there is an obstruction to the circulation through the arteries of the cord as the result of the heaping up of cells in the perivascular lymph-spaces. I fail to see, therefore, how blood-letting, leeches, purgatives and depletion can have any good effect.

In regard to what Dr. Crandall says, my first cases go back about seventeen years, and a diagnosis of rheumatism had often been previously made on account of the pain.

DR. ACKER: I was looking over some records in Washington and found that in 1898 there were more cases than usual and then again in 1903 there were a number of cases, and there was no pain in any of these cases.

We had more than 500 cases in the epidemic in Washington, I am sure. Many of the cases were not reported and many were of the abortive type. I saw altogether about sixty cases. This epidemic started in June and lasted until September. I have not seen any cases of contagion. We put the patients on one side and typhoid cases on the other, and no nurse or mother was infected. If the disease is so contagious I do not understand why the nurses and mothers would not have been infected. In 1904 I reported a case where one brother had the disease in 1903 and another brother in 1904, showing the family predisposition to the disease. In all the cases I inquired about the nasal and throat conditions and only found trouble of this kind in one case, but there was a great deal of gastro-intestinal trouble. The cases seemed to be more like cerebrospinal meningitis; one child had convulsions that lasted twenty-four hours; another child recovered, but later died from the cerebral trouble.

On Wisconsin Avenue, leading out to the country, cases occurred all along the road, but not out in the country.

In regard to treatment, I find that hot baths given during the attacks relieve the pain very much. As to lumbar puncture, in every case in which it was used it

seemed to relieve the pain almost immediately, and I advocate its employment in cases in which there is a great deal of pain.

DR. MACHELL: I would like to ask Dr. Flexner whether it was noticed that cases occurring in this last epidemic were milder than in former years? In Toronto, the cases seemed to be of a rather milder type than previously, and it seemed to occur in younger children. In six days in the early part of September we had a case come into the Hospital for Sick Children each day, and the age of each child was a year or younger. There was this peculiarity, that the first six cases had a peculiar rash, very much like that of chickenpox. I would like to know if that has been general.

DR. LOVETT: In reply to Dr. Churchill's remarks, I know of no explanation as to why there should be so many cases in Minnesota. Swedish immigration has been getting less; it has fallen off since 1905. There is a periodicity about the disease which we cannot explain.

DR. FLEXNER: The question of Dr. Blackader has, I think, been already answered. I am also of the opinion that repeated lumbar puncture could do no harm.

The question of contagion will, of course, very likely be discussed *pro* and *con*. Poliomyelitis is not apparently contagious in the sense or degree of measles and scarlet fever; yet there are many instances in which two, three, and even more cases of the disease have occurred in the one family. I know of one instance only in which nurses became infected while attending cases of poliomyelitis in a hospital. Our attitude regarding the question of contagion should perhaps be similar to that toward cerebrospinal meningitis. It seems established that in hospital practice, where contact is not very intimate, no spread is likely; but the same thing does not apply generally to cases in private practice, and especially in crowded tenements. In the present state of our knowledge we are justified in considering epidemic poliomyelitis as being contagious, and in applying measures based on this consideration.

Dr. Haynes has asked me to say something concerning the question of the persistence of the virus in the body. I have dealt with this matter in the paper so fully that perhaps it is unnecessary to go over it again.

I should like to say finally, in reference to local disinfection, that I fear a 1 per cent. solution of hydrogen peroxide is rather irritating to the mucous membrane of the nose. Menthol is a pretty efficient antiseptic for the virus, and I should be disposed to employ it in the usual combination, particularly because I think that it leads to cleanliness, and I believe that mechanical cleansing is an important factor.

DR. KOPLIK: I do not think the type of the disease is different at present from what it was formerly. To-day cases are included that were formerly not recognized as poliomyelitis.

I would emphasize the point made by Dr. Flexner that we cannot compare the hospital cases with those seen in private life. Although we had no spread of the disease in our own wards, two nurses were infected in the Staten Island Hospital.

DR. KNOX: My opinion as to blood-letting in this condition agrees with that expressed by Dr. Morse. The antibodies are produced in the blood and to remove the substance in which they are produced would be to destroy one of the best means of protection.

An experience last year with urotropin, not in this disease, but in another, was suggestive. In an orthopedic hospital in which an epidemic of measles occurred in a ward, sheltering five or six cases, there was a case awaiting operation for spina bifida, and urotropin had been given for two weeks previous to the operation. This was the only case in that room that did not develop measles. So it occurred to me that possibly the use of some such drug might be of service in preventing the spread of other infectious diseases.

THE POLYGRAPH AS AN AID IN DIAGNOSIS OF CARDIAC CONDITIONS IN CHILDREN *

GODFREY R. PISEK, M.D., AND T. HOMER COFFEN, M.D.
NEW YORK

That there has been no startling advance in our methods of physical diagnosis since the days of Skoda and his pupils will probably not be denied. These men left us a rich heritage, and we are only now, through the use of scientific instruments, blazing new paths and adding valuable record findings to those of the unaided senses.

The use of the polygraph with adults has proved of great value in correlating physiologic and clinical data. It has removed that element which we speak of as the "personal equation," and instead gives records which are true for all time, and only require correct interpretation. These records have stimulated closer study of the heart and the circulation, so that the anatomist, physiologist, pathologist and clinician have all profited thereby and developed newer conceptions of the intricate cardiac mechanism.

The studies of Gaskell, who showed that the heart muscle itself possesses characteristic tone, that it can originate its own stimulus and conduct it to various parts of the heart, explained many of the phenomena recorded in polygraphic tracings. For example, the physiologist now knows that the auricle contracts an appreciable, measurable interval before the ventricle, and that the stimulus which produces cardiac contraction arises at the mouths of the great veins, spreading down successively over the right auricle, thence through the bundle of His and its branches to the ventricles.

Further, it has been shown that a dissociation between auricle and ventricle can be produced experimentally by destroying the tissue at the auriculo-ventricular junction, which contains special muscle and nerve fibers, and which seems to be a "connecting pathway" for the contraction stimulus.

With the polygraph we can show definitely whether the cardiac rhythm is normal; if normal, whether the arrhythmia is due to respiratory or other influences; whether ventricular contraction follows

*Read before the American Pediatric Society, Lake Mohonk, N. Y., June, 1911.

auricular contraction as it should; whether the excitability of the heart is normal. With this instrument it is possible to study the functions of the cardiac muscle, namely, tonicity, rhythmicity, contractibility and conductivity. Thus far, the function of conductivity is best understood, and we find it disturbed in the usual forms of pulse irregularity. A study of the polygraphic tracings tells whether the irregularity is due to heart block, fibrillation of the auricle, or extra-systole, and, if the latter, which one of the three varieties of extra-systole is present. All these facts are of the greatest importance, for we have at hand by this means, in certain cases, just as precise knowledge (of the cardiac function) as one obtains by finding the malarial parasite in the blood-cells.

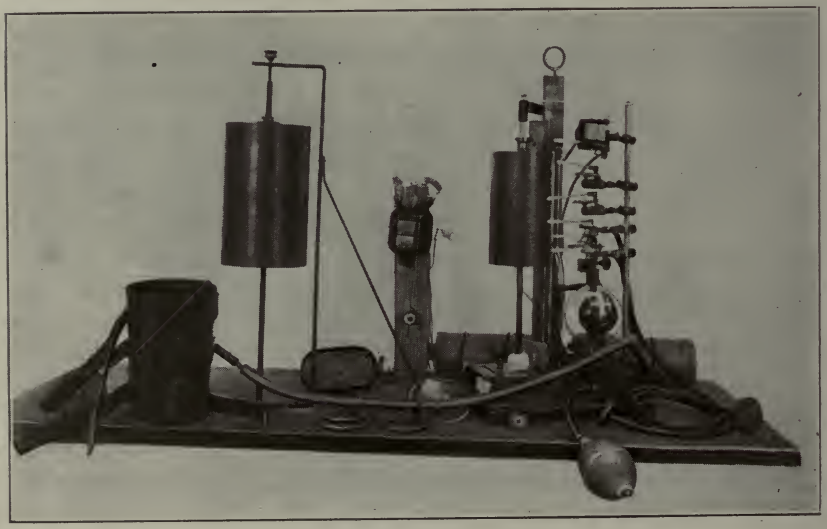


Fig. 1.—Modified Sphygmograph. With this instrument long tracings may be taken of brachial artery, apex, respiration, jugular vein and time (in 1/10 second).

With these facts in mind, we undertook the application of these methods in cardiac conditions in children, to determine (1) if satisfactory tracings could be made from children; (2) if information additional to that obtained in the physical examination was possible; (3) if this information could be utilized in prognosis and treatment.

The instrument used in our work was our modification of the Erlanger sphygmograph with a Hirschfelder attachment (Fig. 1). This

apparatus allows a simultaneous tracing to be made (1) of the pulse — known as the sphygmogram; (2) of the heart — cardiogram; (3) of the venous pulse — phlebogram. These three tracings, when studied in relation to each other, become much more valuable than when taken alone, even with the finest instrument.

The sphygmogram gives information relating to the movements of the left heart, the rate and rhythm of the heart, and the variations in pressure within the artery.

The cardiogram gives the tracings made over the precordium, or apex, and gives exact data concerning the heart movements, and aids in defining the cardiac systole. It should not be forgotten that the

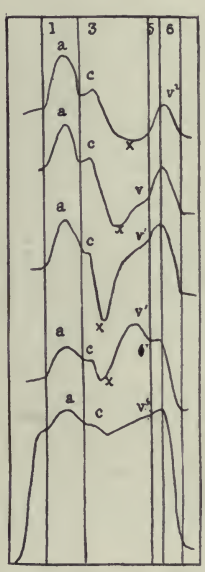


Fig. 2.—The Normal Phlebogram (Hay). Diagram from actual tracings showing the variations in the records of the auricular type of venous pulse. The upper phlebogram is normal, the lowest shows the marked effect of free tricuspid regurgitation in increasing the engorgement of the right auricle. Note the gradual increase of the wave *v* at the expense of the auricular depression *x*. The portion *v'* of the ventricular wave *v* occurs in the phlebogram before the perpendicular line 5.

cardiogram does not record the pressure within the ventricle, but does give information as to the displacement of the heart in relation to the chest wall. It further indicates certain physiologic events which are helpful in determining pathologic states of the heart. In other words,

the cardiogram gives information regarding the duration of the systole and diastole, the beginning of ventricular systole, and indicates the period of the action of the aortic valves and the opening of both cuspid valves. Sometimes the normal type of cardiogram becomes inverted — where there is such marked hypertrophy and dilatation of the right ventricle as to force the left ventricle out of position on the chest wall. How valuable such information may be to the clinician need not be emphasized here, since he may be able to note on subsequent records in convalescence the gradual return of the left ventricle to its place, as shown by a positive cardiogram.

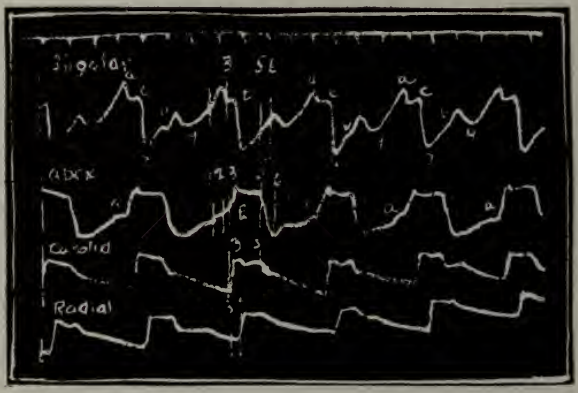


Fig. 3.—Normal tracings from jugular vein, apex, carotid and radial arteries recorded simultaneously (Mackenzie). The line above the jugular tracing is the time in 1/5 second. Note the waves, *a*, *c* and *v*. The beginning of the wave *c* occurs just 1/10 second before the rise (due to ventricular systole) in the radial as shown in line 3 in radial and jugular tracings. The *a* wave, due to auricular systole, begins about 1/5 second before *c* as shown by line 1, in the jugular tracing. This is during the diastole of the ventricle as shown by the falling line in the radial tracing at this time. The beginning of the wave *v*, occurs usually at the beginning of the rise in the radial. Its fall, however, marks the opening of the auriculo-ventricular valves and is coincident with the dicrotic notch of the radial tracing. The jugular pulse varies considerably, but the waves *a*, *c* and *v* can be measured off as has been explained.

The phlebogram is of these three records the most important, as by representing the variations in venous pressure (when taken in the neck), it indicates the activities of the right side of the heart. While in some instances the interpretation of these tracings has led to controversial theories, in the main observers agree, and at all events the records stand ready for any advance in this field of medicine.

In reply to the first problem which we undertook to answer: Can tracings be obtained satisfactorily from children? In our series of cases, the ages of the children varied from 4½ to 15 years, and all were suffering from cardiac lesions, either congenital or acquired. In each case we obtained satisfactory tracings from the brachial artery, precordium and the jugular bulb. With only slight modification of the appliances to

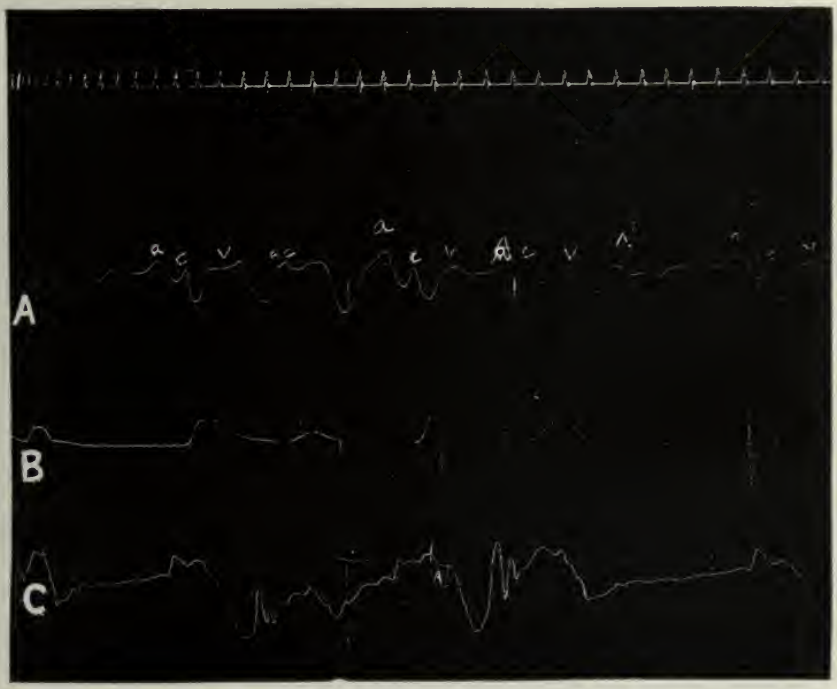


Fig. 4.—Digitalis heart-block, in a boy 15 years old. After stopping digitalis the heart-rate became normal. At A′ in the jugular tracing is evidence of auricular contraction, while there is no contraction of the ventricle. A, right jugular, B, brachial, C, apex curves.

suit the smaller anatomical areas we were able to make records without difficulty. For examples of well-marked jugular tracings in children see Figures 5 to 14 inclusive.

Before taking up the second question, or the value of tracings taken in children, it may be well to review briefly the anatomic and physiologic essentials on which interpretations are made.

The right jugular bulb, which is found to be about one inch outside of the sterno-clavicular articulation, is the point over which the cup is placed to obtain the venous tracing. The right internal jugular, innomi-

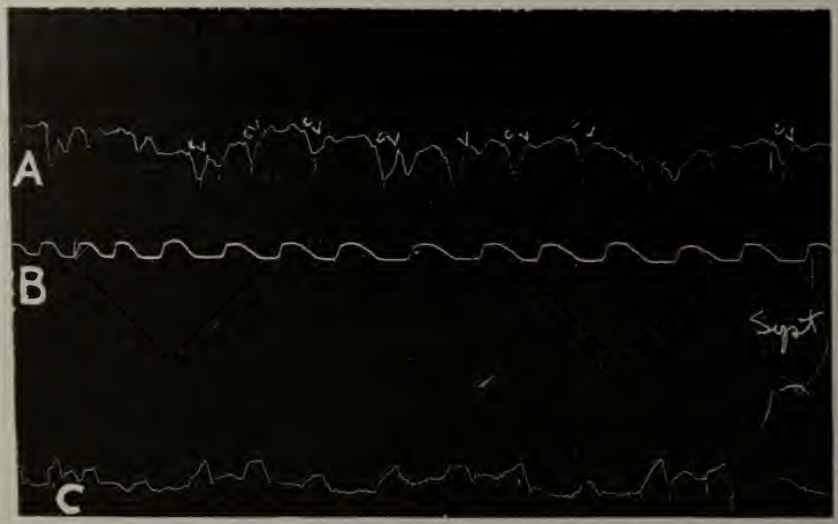


Fig. 5.—M. M., aged 10 years; respiratory arrhythmia; mitral insufficiency. Large jugular tracing, third heart sound. "H" wave in jugular. A, right jugular, B, brachial, C, apex curves.

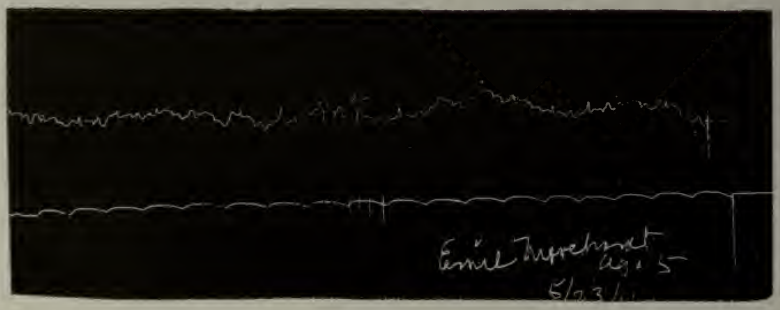


Fig. 6.—E. M., aged 15 years; normal heart; respiratory arrhythmia. Note the large jugular waves in upper tracing.

nate vein, and superior vena cava, extend almost in a straight line from the heart. The pulsations are best obtained by lowering the child's head and placing it in such a position that there is a relaxation of the sterno-

cleido-mastoid muscle. The best point to obtain the tracing from the jugular vein is about three-quarters to one inch external to the right sterno-clavicular articulation.

The normal venous tracing shows three distinct waves, called the (a), (c) and (v) waves (Figs. 2 and 3). The (a) wave occurs early in diastole of the ventricle, as can be seen by placing the hand over the apex and watching the time of this rise in the jugular pulse. The wave, however, is the result of the auricular contraction.

Following the (a) wave, a negative phase is recorded, termed (x), caused in greater part by the diastole of the ventricles, but this is inter-

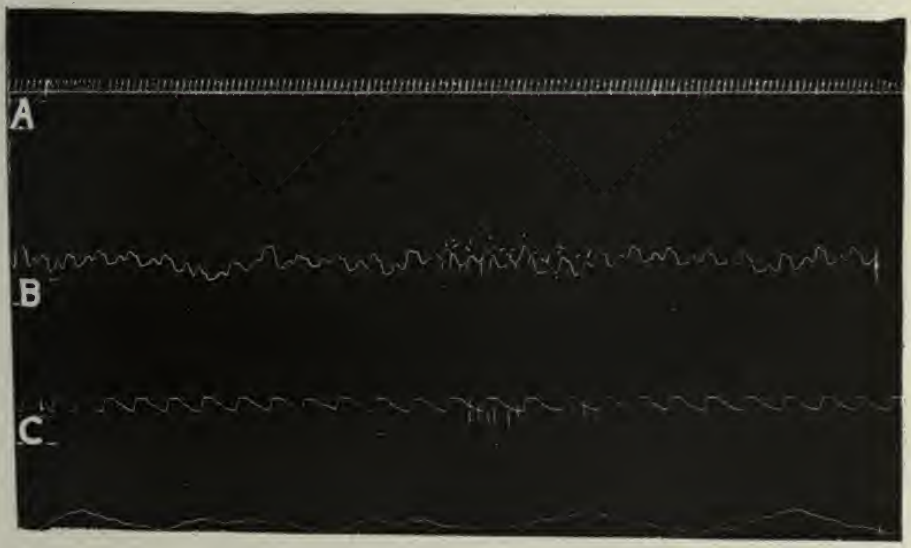


Fig. 7.—B. W., aged 4½ years. Congenital pulmonary stenosis. Note the large jugular waves. A. time, 0.1 second; B, right jugular, C, brachial curves.

rupted by the (c) wave which is synchronous with the carotid pulsation.

The "a-c interval" is almost constant in point of duration, i. e., one-fifth of a second in the normal heart — and indicates the time of passage of the contraction stimulus through the "conducting pathway" (Bundle of His).

The third wave (v) occurs synchronously with the systole of the ventricle. It is increased in size by any factors which tend to more rapidly fill the right auricle, and hence the veins.

A second negative diastolic phase (y) follows the (v) wave and records the emptying of the cervical veins. The importance of noting this wave is seen in cases of engorged right heart with over-distended veins in the neck. In these instances it is found practically absent.

To analyze a tracing from the jugular vein, one must compare it with a tracing taken at the same time from the brachial or radial artery (see Fig. 2). With a pair of compasses, place the left point on the

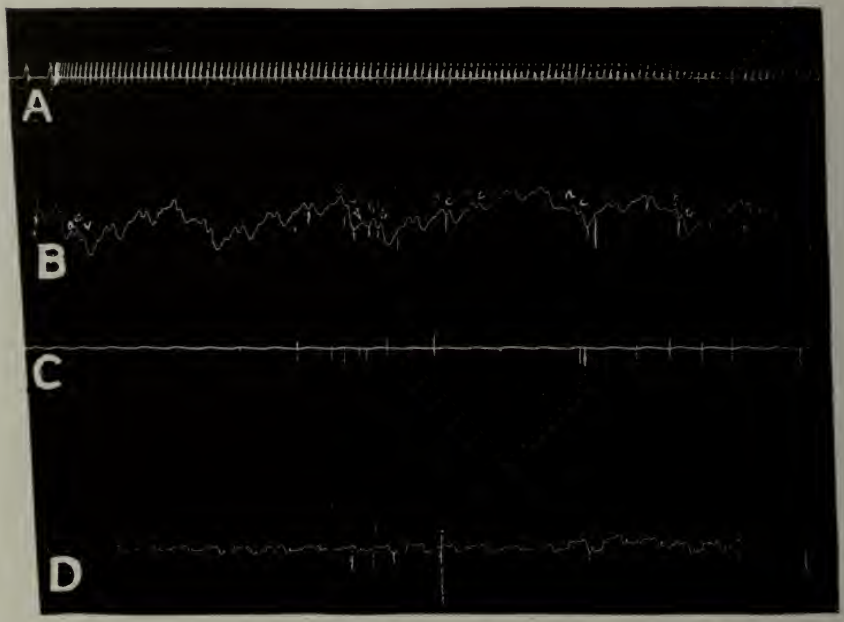


Fig. 8.—M. K., aged 5. Mitral insufficiency—uncompensated. Note large jugular waves and protodiastolic wave in cardiogram (associated with "third heart sound"). A, time 0.1 second; B, right jugular, C, brachial, D, apex curves.

first vertical or base line in the radial tracing; place the other point at the beginning of any rise; then move back the right leg of the compass one-tenth of a second, as indicated on the timer above; then place the left leg on the base line of the jugular, and the right point will fall on the beginning of the rise of the (c) wave. This should be the time for (c) in the jugular tracing, for it occurs one-tenth of a second earlier in the jugular than in the radial. Then measure one-fifth of a second to the left of this (a) wave, which should fall on "a." The wave following (c) is (v).

In interpreting any polygraphic tracing, it is advisable to consider the functions of cardiac muscle, particularly that of conductivity. Cases of Stokes-Adams disease have recently been reported in adolescents, and undoubtedly cases of partial heart-block occur with severe cardiac lesions.

Normally, the a-c interval is of short duration. If the function of conductivity is interfered with, then the passage of the stimulus through the auriculo-ventricular bundle (or bundle of His) is delayed, causing the a-c interval to be lengthened. This form of cardiac arhythmia is

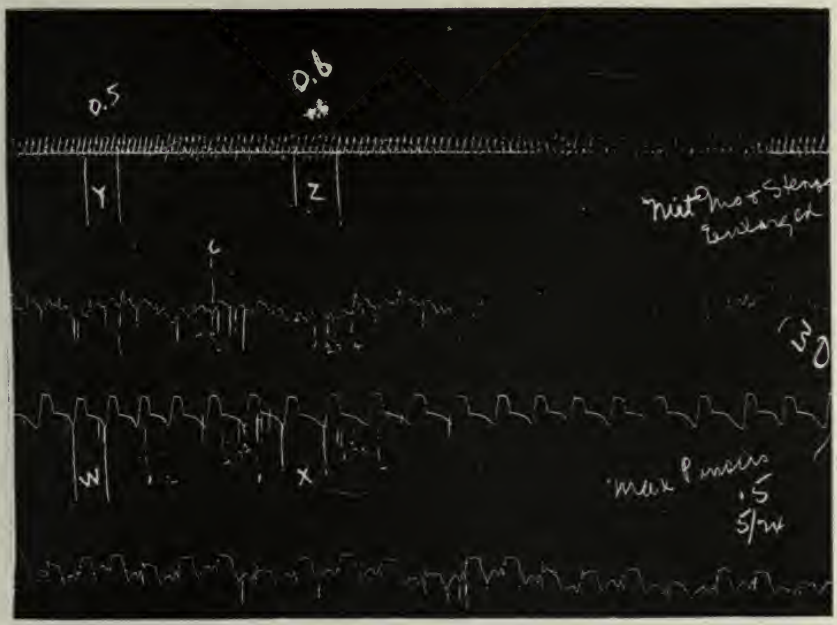


Fig. 9.—M. P., aged 5. Mitral insufficiency and stenosis; cardiac enlargement. Note respiration effect on cardiac rhythm; increased frequency with inspiration, decreased with expiration. Cardiac cycle W. 0.5 sec., cycle X—0.6 sec. Note protodiastolic wave "p" in cardiogram (associated with third heart sound) and corresponding wave "h" in jugular.

found in acute ulcerative endocarditis, and not infrequently in cases of heart-block which have come to necropsy actual destruction of the bundle of His has been found.

If the lesion in this auriculo-ventricular bundle is so extensive as to cause complete "blocking" of the stimulus, then ventricular contraction does not follow that of the auricle, as it normally should, resulting in

what is known as "heart-block." The dissociation between auricle and ventricle may be absolutely complete (the auricle beating independently of the ventricle and vice versa) or the ventricle may beat to every second, third or fourth auricular contraction.

Digitalis is often indiscriminately prescribed to children because they "have a valvular lesion." The polygraph teaches that it should never be prescribed for any individual whose a-c interval is prolonged, since it then only depresses the function of conductivity and accentuates any

Fig. 10.—T. S., aged 7 years. Mitral insufficiency—uncompensated. Note the large jugular waves (B). A, time 0.1 second, B, right jugular, C, brachial curves.

arrhythmia which is present. Such an instance from our series is presented in Figure 4. The patient was a boy of 15 admitted to the hospital with marked decompression. He had been taking digitalis in large doses — 15 minims of the tincture four times a day. On the seventh day the pulse, which had been regular, showed marked arrhythmia. The tracing, Figure 4, was taken on the eighth day, and

shows typical heart block. The digitalis was then stopped, and seven days later his pulse was regular. The cause of such irregularities can best be recognized by the polygraph. Here we have a condition which, if not recognized, may become serious. Ordinary methods of physical examination do not reveal the real condition.

Of the other functions of cardiac muscle, that of stimulus production was found particularly interesting in our series of tracings. In *every case* we found a quickening of the pulse with inspiration and a slowing with expiration. This is known as respiratory arrhythmia (Figs. 9, 5 and 6). That it is caused by irregularly produced stimuli is shown by

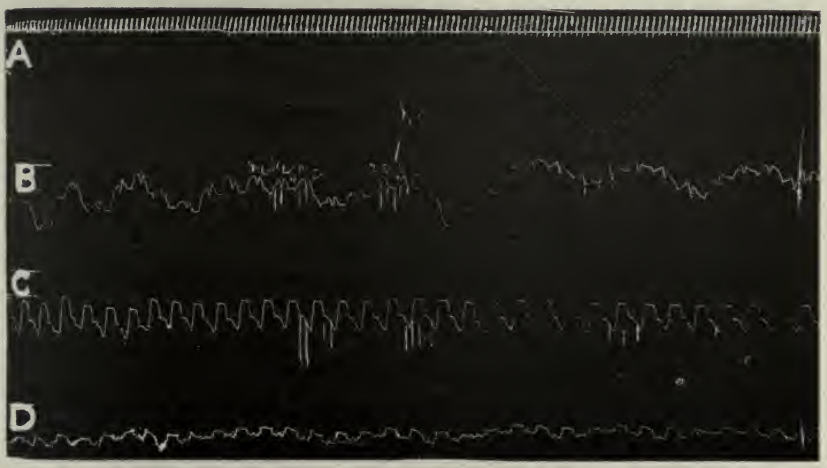


Fig. 11.—L. B., aged 12 years. Neurotic heart. Note character of jugular and cardiac tracings. A well-defined "p" is present in the cardiogram, with an occasional "h" wave in the jugular tracing. A, time 0.1 second; B, right jugular, C, brachial, D, apex.

the fact that ventricular contraction follows auricular contraction normally; in other words, that there is no disturbance of conductivity, an important fact to recognize. The cardiac muscle in neurotic children is particularly predisposed to this disturbance.

No evidences of the function of excitability were noted in our records. This was contrary to our expectations, since the child is apparently susceptible to abnormal or irregular stimuli in other portions of its organism. We concluded, therefore, that the myocardium in the young does not exhibit any extra systoles, even in rapidly beating hearts.

Fig. 12.—G. S., aged 12 years. Mitral stenosis. Note large jugular waves (upper tracing).

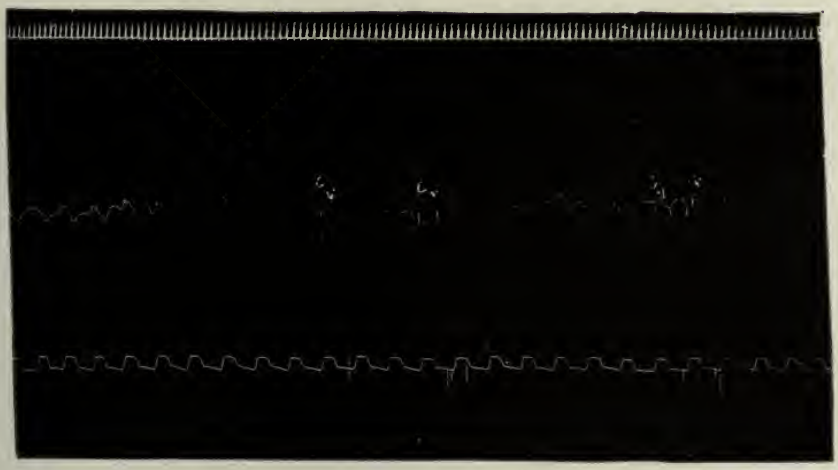


Fig. 13.—E. B., aged 13 years. Mitral insufficiency; overacting heart with slight hypertrophy. Note the excellent jugular tracing with normal *a c v* waves. Auricular type.

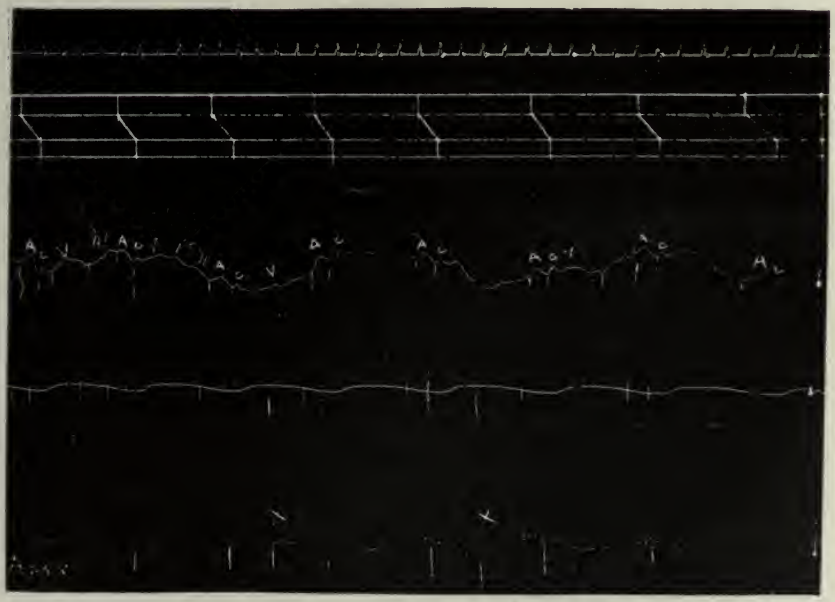


Fig. 14.—T. S., aged 6½ years. Mitral insufficiency and aortic insufficiency. Diagram represents passage of stimuli through auriculo-ventricular bundle. Normal

Another point of interest in our study was the occurrence of the "third heart sound." This is accompanied by characteristic waves in the cardiogram and phlebogram (Figs. 5, 8, 9, 10). The significance of this is as follows:

In some cases the existence of this extra heart sound was not noted on the preliminary physical examination, and it was only recognized after its appearance on the tracing had specifically called our attention to its presence. Thayer states that it can be heard at the apex in about 30 per cent. of normal individuals, when they are lying on the left side. In the first decade it occurs in 58.9 per cent. of cases.

This protodiastolic wave in the cardiogram is associated with an extra wave (h) appearing soon after the (v) wave in the jugular tracing (Figs. 5, 8, 9, 10) and therefore occurs in the early filling of the heart; in other words, at the very beginning of diastole. At this time the mitral and tricuspid valves are closed by the elastic recoil of the heart walls. Hirschfelder believes that it is due to the sudden snapping together of these valves. This wave may be pronounced whenever there is a ventricular distention — as in dilatation following hypertrophy, in stenosis of the mitral valve, and in aortic insufficiency, in which there is found to be an increase of intraventricular pressure. It is always accompanied by a wave designated as "p" on the cardiogram.

CONCLUSION

When making a physical examination of a patient with heart disease, perhaps the least important for the patient is the determination of the precise valve involved. The examiner should endeavor to determine the exact power of the heart to respond, to study the functionating ability of the myocardium and obtain data of the cardiac activity. These facts, in conjunction with the physical findings as to size, possible dilatation, or organic lesion, enable the physician to form a much more precise opinion as to the prognosis, while his treatment, at least, is based on scientific facts and can be controlled by further observations.

The results of our study may be summarized as follows:

1. Tracings satisfactory for diagnosis can be obtained in children.

2. The polygraph offers a means of accurate diagnosis which is not afforded by ordinary methods of examination, and should be used in addition to these — it will not replace them.

3. The information obtained from polygraphic tracings is of value for prognosis and treatment. Digitalis heart-block should be suspected where the pulse becomes irregular under the use of this drug.

4. Respiratory arrhythmia was found in our series with surprising frequency. This is said to be physiological, but we are led to suspect that it may frequently be misleading, and that the physician may suspect serious cardiac weakness. This was illustrated in cases of scarlet fever, diphtheria and measles studied by us at the Contagious Hospital. The "irregular hearts" were shown to have marked respiratory arrhythmia. We have yet to find extra systoles or auricular fibrillation in children.

The use of the polygraph will not stultify physical findings; on the contrary, more careful examinations will be made, for its use enhances their value and interprets observations which have thus far been unexplained.

DISCUSSION

DR. LA FÉTRA: I wish to report a case of heart-block occurring in a child 8 years old. Such cases are very uncommon. This patient came to the Vanderbilt Clinic last November because of some mild disturbance, bronchitis, I think, and on examining her in the routine way we found that she had a pulse of only 40 which called our attention to the fact that there was something very peculiar about the child. We have no polygraph at the Vanderbilt clinic and so she was sent to Mt. Sinai and the Presbyterian, and at the latter place Dr. James studied her curves carefully and found that she had a partial heart-block, with two auricular systoles to one ventricular; the auricular eighty to the minute and the ventricular forty. In seeking the possible cause of this condition it was found that three years previously she had had a severe attack of diphtheria with some paralysis, and it is possible that this caused some disturbance of the bundle of His, preventing complete conduction. One similar case has been reported. This case will be reported in full later.

DR. JACOBI: I would particularly emphasize the neglect we have shown for a long time of diseases of the myocardium. You will probably remember from the history of heart disease that the myocardium was conceded to be an important factor only in the last twenty-five or thirty years. We know more about the myocardium now than formerly, and that is one of the valuable suggestions in this paper. On the other hand, we are in danger of overdoing it. Formerly we made only a diagnosis of endocarditis; now we are too apt to make only a diagnosis of myocarditis. That would be a mistake. I am afraid our attention has been turned too much in that direction. A good deal depends on which valves we have to deal with. We have all had the experience that in chronic aortic disease, particularly, digitalis and strophanthus will do little for us and are almost always contraindicated.

DR. PISEK: I am glad Dr. Jacobi brought out that point for I do think we could swing the pendulum too far the other way. I wish to state that before making any extended or detailed reports we would like to continue the study a year or two longer, especially in cases of diphtheria and scarlet fever, for here it is particularly important to determine that there is no obstruction to the conductivity or to the essential functions of the heart. Many accidental murmurs have been regarded as grave conditions, and these indeterminate cases can be correctly analyzed. Dr. LaFétra's case is, I believe, one of the youngest on record.

REPORT OF A CASE OF DIABETES MELLITUS IN A CHILD UNDER ONE YEAR OF AGE

PERCIVAL J. EATON, M.D., AND E. B. WOODS, M.D.
PITTSBURGH

The child whose case we wish to report was born in the country about 40 miles from Pittsburgh, and was brought to us by Dr. J. C. Stahlman of Vandergrift, Pa., to whom we are indebted for much of the history, for many analyses of the urine, and for details of treatment. The child visited us first on Feb. 6, 1911, and presented the following:

Family History.—Grandmother on mother's side died in 1908 of diabetes mellitus. Father and mother rather undersized, spare; apparently in good health. No specific history. Father has had chronic appendicitis eventuating in excision. One older child died of chronic appendicitis August, 1909, ill four months; and this child was born ten months later in June, 1910. The mother had acute indigestion during the last two months of gestation, and for one month after delivery. The father's family are all of constipated habit. There have been no marriages of relations on either side so far as known. The specimens of urine of both father and mother were analyzed May 26, and found free from sugar.

Previous History.—The child was instrumentally delivered, and had some lesion over left eye which took five or six weeks to heal up. Baby breast fed, and appeared to thrive well till December, 1910, when it was brought to Dr. Stahlman because of the appearance of a swelling on the third toe of the left foot. There then was a minute vesicle on second joint, and, thinking it the result of an infection, a boric acid lotion was used. The following week the fourth toe on the right foot presented a similar appearance. The toes were reddened and swollen, but apparently not painful to the touch. The child manifested no symptoms of illness at this time. It had been making a gain of from 1½ to 2 pounds per month, and about Jan. 7, 1911, weighed 16½ pounds. It was now about 7 months old and had cut two teeth. The toes remained in the same condition as above noted, no treatment appearing to affect them. About January 15 the mother noticed that the child's diapers were sticky after urinating, and stiffened on drying. About January 20 the mother collected an ounce of urine, and Dr. Stahlman found it to have a specific gravity of 1.035 and a very decided sugar reaction, using the Haines reagent. On January 21 another specimen had a specific gravity of 1.037,

with sugar reaction marked. Repeated examinations at short intervals gave specific gravities of from 1.016 to 1.035, most often about 1.026; acetone present in all specimens after the first two or three weeks and occasionally diacetic acid. The specimen examined by Dr. Stahlman previous to his last report to us was on April 22, when the specific gravity was 1.021; some acetone, but no diacetic acid. Our own examinations up to this time (April 22), and later, have confirmed these findings. The first specimen was examined by us on February 6; specific gravity, 1.030; no albumin; sugar present. On February 13 a second specimen was received; specific gravity, 1.032; no albumin, and with a typical reaction for grape sugar; acetone and diacetic acid present. Saccharometer reading over 10 per cent. (fermentation test). March 2, specific gravity, 1.030; no albumin; grape sugar present; acetone and diacetic acid present.

For a time there was thirst and increased diuresis, but under date of Feb. 9, 1911, the mother writes me that the child was losing his appetite and did not care for water, taking only about an ounce a day. The child began to lose weight early, and about March 15 had lost 2 pounds, 6 ounces.

On February 6 (the date of the child's first visit to us), we had suggested that the child have breast milk only, as for several weeks it had had oat-jelly in addition. At that time, too, it was given some gray powder and iodid of iron. After using the iron and gray powder for about four weeks and seeing no result, Dr. Stahlman put the child on bicarbonate of soda with one-tenth grain codein and trypsogen tablets, starting with one-half a tablet three times a day and increasing to one tablet three times a day. About March 8 he began feeding a washed cream mixture in addition to the breast. This mixture seemed to work well, and has since been continued. On March 26 it was found to have gained 4 ounces; April 9, 2 ounces; April 30, 2 ounces. Under date of May 2 the doctor writes that in addition to 24 ounces of this washed cream mixture it is taking some meat broth. Up to the time of administering these foods the child was very restless, especially at night, but latterly has been less disturbed, though it demands and gets the breast several times during the night. Regularity of feeding has not been attained. The child has been very constipated and has had to have milk of magnesia and enemas. Later was given cascara, which seemed to give good results.

On May 22 Dr. Woods and myself visited the child at its home and found it in very fair condition. It weighs 14¾ pounds, and is very active

physically and very bright mentally. Though the weather has been very hot and sultry, its thirst has not been appreciably increased — it rarely taking more than an ounce of water at a time. Just now its bowels are in good order, the trypsogen having been omitted, apparently having had no effect on the disease and probably causing constipation. At all events, since omitting it, the bowels have moved spontaneously. The toes are no longer red, but are still swollen and rather fusiform in shape. The child's color is fairly good. It has been having breast milk, beef juice (the meat broths not now being relished) and the washed cream mixture. This latter is prepared by allowing a quart of milk to stand twelve hours, then removing all the cream, shaking this in a Mason jar with an equal amount of water, then allowing the cream to again rise, and, after skimming the cream, making thereof a mixture one part to four of water, adding a bit of saccharin and a little (indefinite) amount of lime water. The child rarely takes more than 5 ounces of this mixture at a feeding.

We brought home a specimen whose specific gravity was 1.044, no albumin, sugar present, acetone present, diacetic acid absent, microscope negative. (Fermentation test, 5½ per cent.) Dr. Stahlman has sent under date of May 27 the report of a specimen examined by him, which showed specific gravity, 1.044; albumin, none; sugar present by Nylander's and Haines' reagents; acetone present; diacetic acid absent; no odor. (Fermentation test about 7 per cent.) Dr. Stahlman also reports that the child has not been resting so well the past week, and that it does not take its food well, the feedings having to be forced. The hot days seem to affect it a good deal.

In reviewing the literature of the past fifteen years we have been able to collect reports of 647 cases of diabetes mellitus in children, and of these but seven were under 1 year of age. We have been able to discover but four more cases to add to the above, namely, in children under 1 year.

In 1901 Young reported a case of a 6-months-old infant and Orloff of a 4-months-old infant.

In 1910 Lauritzen reported a case of an 8-months-old infant and Maurel of a child under 1 year.

In 1899 Hagenback collected seventy-seven cases of diabetes mellitus in children under 1 year, but we have been unable to find reports of these cases. Excluding Hagenback's series we have only been able to collect eleven cases of diabetes mellitus in children under 1 year.

In discussing the subject of diabetes mellitus we wish to draw attention to the fact that small quantities of milk-sugar may appear in the

urine of breast-fed and bottle-fed children, especially in the latter class of cases, where milk sugar is added to the food. Sugar excreted under these circumstances has no pathologic significance in so far as diabetes mellitus is concerned, but must be differentiated from grape sugar. Attention must also be given to the fact that transitory glycosuria occurs much more often in children than in adults, and is supposed to be due to an impairment of the function of the pancreas due to some intoxication. In a case such as is here reported it is, for the matter of prognosis, very desirable to be able to decide whether a given case is true diabetes mellitus or merely a transitory glycosuria. Though the case reported has continued for more than four months, and though the symptom-complex is fairly complete, yet the absence of increased thirst and diuresis makes us doubtful, or at least causes us to refrain from giving an absolutely unfavorable prognosis.

Etiology.—This has been so fully discussed in the literature that here reference will be made only to a few points. Heredity, which is dwelt on at length by some authors, has apparently little to do with our case. There is no family diabetic habit, so far as we can tell, and we have no reason to suppose that the older child in this family died of diabetes mellitus. There have been no consanguineous marriages, nor is there any ground for suspecting syphilis. There remains of interest to us only the question of the effect of traumatism, and we know there was a rather bad left side lesion at birth. The head now seems to be normal.

Symptomatology.—The existence of thirst, diuresis, wasting of the body and the stiffening and stickiness of the linen, accompanied by the excretion of grape sugar, make up the complete symptom-complex.

Prognosis.—It seems to be the consensus of opinion that the prognosis in true diabetes mellitus in children is absolutely bad, and that the duration of the disease is rarely more than twelve to eighteen months.

Treatment.—So far as we have been able to learn, no drug or combination of drugs has so far had any effect on the disease, and the only philosophic treatment would seem to be the exhibition of such dietetic and hygienic measures as would tend to keep the child in the best possible physical condition.

DISCUSSION

DR. JACOBI: The New York Academy of Medicine Library contains a number of books and pamphlets, more than a hundred, I believe, each one describing at least one case of diabetes mellitus in children; among them are a few cases of about the same age of the patient whose case Dr. Eaton reports. One of the cases he will find described in the *American Journal of Obstetrics and Diseases of Children*,

in one of the first volumes; not later than the third. It dates back to 1869 or 1870. That case I saw with Dr. Brown, whom some of you will remember as an assistant of Dr. Gaillard Thomas. The patient died very soon. They do not live long; one year or eighteen months; usually they die within a short time; even children of 10 or 15 years die very soon. I have seldom seen one live over a year. Still there are cases on record that are reported to have recovered. About ten years ago I saw in one family two boys of 5 and 7, who had been having diabetes mellitus for some time. I saw the two cases twice. They had a sugar percentage of between 3 and 6. One of these boys stopped me in a public place about a year ago to speak to me, a strapping fellow of 16 or 17. I asked him, what is the percentage now? He said 3 per cent. So that he is about with diabetes mellitus. I do not know why. Both of them are in good health. Of course, that is very encouraging and we should not let up on such cases.

DR. EATON: I wish one of the members of the Society would give us some hint as to the treatment of these cases. In regard to length of time these children live, the statistics refer almost entirely to much older children. I had nothing to go on for a prognosis, as to how long a time the child might live. I read somewhere of a father and two sons having the disease, I think the sons were 25 or 30 and the father 20 or 30 years older. They had established a tolerance for certain amounts of carbohydrate, and by careful diet could keep the percentage of sugar down. One of the remarkable things about this child is the variation in the amount of sugar without any apparent cause. Twice we found nearly 10 per cent. Such cases are extremely rare and this one will be particularly interesting to follow because the child is so well, and if the hot weather does not kill it, I think it will live a good while.*

DR. KERLEY: Two cases Dr. Jacobi spoke of have been my patients for several years. The sugar in these two boys was discovered by accident. The mother, a very careful woman, sent four specimens of her four supposedly healthy children for examination and we found that two children, both boys, one 4 and the other 6 years of age, showed sugar in considerable amount. Since this time they have grown and developed into strong, vigorous youths. Both are athletes and are very large for their age. The older boy stands 6 feet, and weighs about 170 pounds. Sugar has been present in the urine in quantities ranging from 3 to 7 per cent. for the past twelve or thirteen years. It appears to have caused no inconvenience. These are not cases of diabetes mellitus. They show no sign of illness whatever. I have seen many other cases of diabetes in children and all were fatal cases who showed the usual typical clinical picture. The patients have been on as careful a diet as is possible to carry out in growing boys. Mental or physical work does not influence the sugar output.

DR. JACOBI: Dr. Eaton asked the question, What can be done? I have done what I do in adults. We get good results with adults. The drugs I have been using are four; salicylic acid, continued for a long time, and used with bicarbonate of soda; arsenic, in larger doses than it is usually given, and highly diluted; codein, which is my preference, and atropin in large doses. Atropin is tolerated in much larger doses by children than by adults.

---

* June 27, 1911, a letter from Dr. Stahlman states that about June 10th. the baby had an abscess in the left side of neck, which was incised and drained. The baby was very weak at this time, but had improved very rapidly. Had cut four teeth within the mouth. Bowels regular; sp. gr. of urine, 1.024; some acetone and diacetic acid present.

HIPPURIC ACID IN THE URINE OF NORMAL BREAST-FED INFANTS *

SAMUEL AMBERG, M.D., AND J. H. MASON KNOX, JR., M.D.
BALTIMORE

The urine of the normal breast-fed infant is mainly distinguished by negative characteristics. This is a statement made by Mayerhofer[1] in his recent paper. In this paper attention is called to the absence of such substances as glycuronic acid, indican, urobilin, etc., in the urine of these individuals. According to the same author some of the products normally encountered in the urine of adults, like the substances paired with glycocoll, namely, benzoic acid, etc., have not been made the subject of detailed investigation. With regard to the occurrence of hippuric acid in the urine of infants, only a few scanty references came to our notice. Marchand[2] as well as Meissner and Shephard[3] state that the occurrence of hippuric acid in the infant's urine is a well-known fact. Amberg and Morrill,[4] examining 260 c.c. of a mixed urine obtained from several healthy breast-fed infants, were unable to demonstrate the presence of free or combined benzoic acid. From the examination of this amount of urine of such low concentration no definite conclusions could be drawn. It was therefore thought advisable to repeat the examination with a larger amount of urine. Thanks to the kindness of Dr. Williams of the Obstetrical Department, we were able to collect about 1,900 c.c. of urine from normal breast-fed infants. The amount obtained from the different babies was as follows:

Infant	Collection started, days after birth	Urine Collected, days	Amount collected, c.c.
1	10	2	409
2	6	6	426
3	6	6	914
4	23	2	162
			1,911

* From the Department of Peditatrics and the Department of Pharmacology, Johns Hopkins University.

1. Mayerhofer: Chemische Teilerscheinungen im Harne gesunder und kranker Säuglinge, Ztschr. f. Kinderh., 1911, i, 487.

2. Marchant: Ueber die Oxydationsproducte des Leims, etc., Jour. f. pract. Chem., 1845, xxxv, 309.

3. Meissner and Shephard: Untersuchungen über das Entstehen der Hippursäure; Hanover, 1866.

4. Amberg and Morrill: Ein Stoffwechselversuch, etc., Jahrb. f. Kinderh., 1909, lxix, 280.

The babies had surpassed their birth weight when the urine was collected and were in perfect condition clinically. To exclude the possibility of slight digestive disturbances 10 c.c. of each sample of urine was used for the determination of phosphoric acid. Moll[5] has shown that the amount of phosphoric acid excreted in the urine of breast-fed infants may serve to indicate very slight digestive disturbances. Only such urine was used as corresponded to the standard established by Moll for the urines of the class "free from phosphates." Therefore we have reason to assume that the urine examined by us was obtained from perfectly healthy individuals.

The method of analysis employed is that of Jaarsveld and Stokvis,[6] which was retested by Van de Velde and Stokvis.[7]

It is not our purpose to discuss here the literature concerning the occurrence of hippuric acid in the urine of animal and man under different conditions, nor the various methods for its determination. References to the literature may be found in the report of the United States Department of Agriculture.[8]

Each portion of urine was immediately evaporated to a small volume with the addition of some sodium carbonate, transferred to a flask and preserved with toluol until the total amount was collected. The method of analysis may be described briefly. The urine evaporated to a small volume is acidified with hydrochloric acid and thoroughly extracted with acetic ether after standing twenty-four hours. The acetic ether extract is washed with water and evaporated at room temperature, the residue containing free and combined benzoic acid, if any is present. The free benzoic acid is extracted with petrol ether. The residue is hydrolyzed by boiling with strong sodium hydroxid, thus liberating the benzoic acid from hippuric acid. After cooling, the fluid is acidified with hydrochloric acid and after standing over night, thoroughly extracted with petrol ether. This extract is evaporated at room temperature, leaving the benzoic acid.

Examined by this method, the urine did not show any crystals on evaporation of the acetic ether extract, nor was any benzoic acid found

5. Moll: Die klinische Bedeutung, etc., Jahrb. f. Kinderh, 1909, lxix, 129.

6. Jaarsveld and Stokvis: Ueber den Einfluss der Nierenaffectionen, etc., Arch. f. exper. Path. u. Pharm., 1879, x, 268.

7. Van de Velde and Stokvis: Experimentelle Beitrâge, etc., Arch. f. exper. Path. u. Pharm., 1883, xvii, 189.

8. The Influence of Sodium Benzoate on the Nutrition and Health of Men, Bull, 88, U. S. Dept. Agriculture, 1909.

after the hydrolysis of the residue from this extract. There was no evidence of the presence of either free or combined benzoic acid. As with other methods of hippuric acid determination in urine, small amounts may escape detection. We may mention the statement of Wiechowski[9] that the method of Jaarsveld and Stokvis gives good results even in the presence of small amounts of hippuric acid.

Since the question of the presence or absence of hippuric acid in the urine of the normal breast-fed infant is of considerable interest, it would have been desirable to extend our investigations with the employment of different methods of analysis, but we were unable to obtain the necessary amount of urine. Nevertheless, from the result just recorded it does not seem probable that a very appreciable part of the nitrogen contained in the urine of the normal breast-fed infant is excreted in the form of hippuric acid.

The character of the food — mother's milk, with its content of lactalbumin — is such that it could supply sufficient glycocoll for the formation of hippuric acid. But even if the food should not yield glycocoll on decomposition, this substance could be furnished by the animal organism. For instance, Grosser,[10] feeding young goats with casein and giving benzoic acid, found hippuric acid in the urine. Furthermore, Brugsch and Hirsch,[11] as well as Feigin,[12] found hippuric acid in the urine of hunger artists. To demonstrate that the normal breast-fed infant can readily furnish glycocoll, such a baby received 0.5 gm. of sodium benzoate. During the next twenty-four hours 175 c.c. of urine were collected, yielding, on evaporation of the acetic acid ether extract, hippuric acid.

The absence of demonstrable amounts of hippuric acid from the urine of the normal breast-fed infant depends, therefore, on the absence of benzoic acid. Most authors agree that the benzoic acid normally entering into the production of hippuric acid in man is either derived from benzoic acid or related substances contained in food, or from putrefactive

9. Wiechowski: Die Gesetze der Hippursäuresynthese, Beitr. z. chem. Physiol. u. Path., 1906, vii, 204.

10. Grosser: Beitrag zur Bewertung des Albumingehalts, etc., Jahrb. f. Kinderh., 1911, lxxiii, 103.

11. Brugsch and Hirsch: Gesammt N, etc., Ztschr. f. exper. Pathol. u. Therap., 1906, iii, 638.

12. Feigin: Ueber die Hippursäurenscheidung, etc., Inaugural dissertation, Berlin, 1906.

processes in the intestinal canal.[13] Since it is known that putrefactive processes are, as a rule, in abeyance in the intestinal canal of perfectly normal breast-fed infants, the absence of hippuric acid from the urine would not be surprising. Quite recently Simon,[14] using the method of Henriques and Soerensen,[15] claims to have demonstrated the presence of hippuric acid in the urine of the breast-fed infant. In this method the hippuric acid is also extracted with acetic ether. The residue is decomposed with hydrochloric acid and the nitrogen of the resulting glycocoll is determined by means of the formol titration. In the first three days after birth the hippuric acid excretion was found to be rather high, running later on a lower level. The lowest figure was found on the eighth day (case Brunner), when 225 c.c. of urine yielded 0.005 gm. of nitrogen, corresponding to 0.0639 gm. of hippuric acid. The urine of our infants was collected later than the third day after birth; that is, when the excretion of hippuric acid has reached a lower level. If we calculate the amount of hippuric acid that should be present in the 1,911 c.c. of urine, using the lowest figure given by Simon, we should have 0.543 gm. of hippuric acid, or 0.37 gm. of benzoic acid. It is very unlikely that the urine examined by us should have contained an amount of hippuric acid approaching such a figure.

13. See, for instance, Baumann: Die aromatischen Verbindungen, etc., Ztschr. f. physiol. Chem., 1886, x, 123; Gerhardt: Ueber Darmfäulniss, Ergebn. d. Physiol., 1904, iii, 138.

14. Simon: Zur Stickstoffverteilung im Urin des Neugeborenen, Ztschr. f. Kinderh., 1911, ii, 1.

15. Henriques and Soerensen: Ueber die quantitative Bestimmung, etc., Ztsch. f. physiol. Chem., 1909, lxiii, 27.

A PREPARATORY STUDY OF THE BACILLUS ACIDOPHILUS IN REGARD TO ITS POSSIBLE THERAPEUTIC USE

THOMAS MORGAN ROTCH, M.D., AND ARTHUR I. KENDALL, PH.D.
BOSTON

The recent advances in our knowledge of the biology of the gastro-enteric tract have been so great that it seems time to begin a study of the practical use which can be made of individual organisms. Prominent among these organisms in the intestine is the obligate member of the acidoduric group, the *Bacillus acidophilus.*

It is to be noted in a general way that (1) this bacillus is a carbohydrate saprophyte; (2) it does not produce toxins; (3) it is a fermental organism, by fermental meaning an organism capable of breaking up the carbohydrates; (4) its habitat is the large intestine; (5) it thrives on carbohydrates, especially the sugars, such as dextrose, lactose and maltose; (6) it produces relatively large amounts of lactic acid from fermentable sugars; (7) it is antagonistic to the proteolytic organisms producing putrefaction, provided sugar is present; (8) although it produces acid it grows best when the medium is less acid; (9) it appears to grow better below the ileocecal valve than above; (10) it is of interest clinically because, under suitable conditions, when the host is placed on a carbohydrate diet, the organism becomes more abundant and it inhibits and even replaces to a considerable extent the bacteria characteristic of a protein regimen (this replacement of the protein flora by acidoduric bacteria is accompanied by the gradual diminution and even disappearance in the urine of those substances which are the products of protein decomposition in the intestine); (11) the *B. acidophilus* is non-pathogenic for experimental animals and under normal conditions is found to be an inhabitant of the intestinal tract of man; (12) it has the ability to render that portion of the intestine where it is localized unfavorable to the development of foreign invading bacteria, and (13) it can form a considerable amount of acid from carbohydrates, forming this acid mostly below the ileocecal valve.

In this same acidoduric group the *B. bulgaricus* has somewhat different characteristics. Its habitat is chiefly above the ileocecal valve, so that

the acid which it produces must be transported to the large intestine and must act at a distance from the chief site of putrefaction and is, therefore, probably less effective than if it were generated at the seat of infection. Its action is most pronounced above the ileocecal valve and grows less as it approaches the anus and the bacilli are only sparsely found in the feces.

In contradistinction to the acidoduric group of intestinal bacteria are the proteolytic bacteria and their characteristics are suggestive of the antagonism which exists between the two groups. (1) The putrefactive (proteolytic) organisms attack and thrive on the protein elements of the food; in certain instances some may become invasive. (2) They may develop toxins. (3) The end products of protein break-down of certain of these organisms are found in the urine and appear as aromatic bodies, these bodies acting as evidence of proteolytic intestinal activity and in some measure acting as indices of such activity. (4) The habitat of this group is said to be chiefly in the large intestine and they are consequently more likely to be abundant below the ileocecal valve. (5) They flourish and increase best in an alkaline or neutral medium. (6) They are inhibited by an acid medium especially by the presence of lactic acid. (7) Certain of these proteolytic bacteria are facultative and as a rule when protein and carbohydrate substances are present they attack the latter first and spare the former. (8) The addition to the diet of easily fermentable carbohydrates, together with restriction of protein food. is of material assistance in reducing the output of these putrefactive products. This results also in the diminution of the activity of the bacteria producing them.

There appears to be a considerable number of intestinal disturbances associated with the activities of putrefactive bacteria, some of which may be influenced by the activity of the *B. acidophilus*. As a well-known example of such putrefactive condition we might mention bacillary dysentery. There are three prominent bacilli which are associated with the clinical symptoms of bacillary dysentery: *B. coli*, streptococci and *B. dysenteriæ*, one or both types. So far, however, as the clinical picture of bacillary dysentery is concerned a differential diagnosis between these organisms cannot be made. The actual recognition of which of these organisms is producing the disturbance is dependent on the bacteriologic examination. Hitherto bacillary dysentery has been regarded as a disease brought about solely by the action of the dysentery bacillus. Now, however, it appears in most cases, at least, that the three organisms mentioned

above working symbiotically in appropriate intestinal conditions produce the symptom-complex of bacillary dysentery.

It is to be noted here that in those instances in which the acidoduric group of organisms has produced lactic acid in considerable amount (through the influence of a carbohydrate diet), *B. coli,* in virtue of its being a facultative organism, changes its metabolism from the proteolytic to the fermentative type. In consequence of this change in metabolism from the putrefactive to the fermentative type, this organism (*B. coli*), which on the protein regimen produced putrefactive products inimical to the patient, and which was, therefore, a symbiote of the dysentery bacillus, now becomes an antagonist to it by forming lactic acid.

In like manner, although we do not know so much about the antagonistic action in this connection, it has been observed that the disturbing streptococci are lessened in number apparently by the action of the lactic acid. It has also been shown in regard to *B. dysenteriæ* that certain changes in its action are brought about by the influence of the change to the carbohydrate type of diet. These changes, so far as is at present known, are as follows: The bacillus, whether of the Shiga or Flexner variety, is normally of the proteolytic type, and, having gained entrance to the intestinal tract, locates itself chiefly below the ileocecal valve. It begins its attack on the protein in the intestine and produces toxins. The bacilli may penetrate the mucosa and even the tissues as far as the mesenteric lymph-nodes and thus establish the bacillus as an infectious organism. The toxins are absorbed and especially affect the anterior horns of the spinal cord.

It is evident that any beneficial therapeutic action on the infectious organisms, so far as the action of the acidoduric group on them is concerned, is to diminish their numbers and to prevent their production of toxins by rendering the medium in which they are growing unsuited for their continued development, thus reducing the amount of toxin which they produce. The damage brought about by the toxins already absorbed cannot be undone. Early inhibitory action of the acid-producing bacteria is therefore indicated.

It has been noted in the changes in flora which take place in the intestine, when by any means the putrefactive types of organisms are gradually changed to the fermentative type, that during the process the bacterial flora first returns practically to a normal type for the nursling, namely, to *B. bifidus* mostly, and to *B. acidophilus* to a degree. Then, as the carbohydrate of the diet is increased the acidophilus increases in

number and greater amounts of lactic acid are produced. Care, however, must be taken not to allow the acidophilus to flourish to such an extent as to establish an acid intolerance in the host.

To be mentioned as of especial significance in an investigation of this kind are certain known possibilities in connection with influences which may be brought to bear on the intestinal flora, and changes which may be accomplished by varying the quality of the food presented to intestinal organisms.

The character of the intestinal flora of man, both with respect to the types of organisms represented, and to the nature of the resulting chemical activities, depends largely on the composition of the diet of the host. A moment's reflection will convince one of the accuracy of this statement; the intestinal bacteria, to a very considerable extent, derive their sustenance from the food in the alimentary canal, and as the food varies, so will the bacteria vary.

This variation in the nature of the bacteria comprising the intestinal flora can conceivably change in two distinct directions, following alternations in the host's diet: either the organisms representative, for example, of a protein regimen may be replaced by an entirely new flora when the host changes his diet to one potentially carbohydrate, or the bacteria characteristic of the protein flora can shift their metabolism to meet the new conditions established by the carbohydrate regimen. As a matter of fact, both possibilities are realized, so that we may recognize three distinct classes of bacteria when the food of the host varies from a protein to a carbohydrate diet. We recognize first an obligate proteolytic group of bacteria, which thrive on a protein regimen. These organisms, best exemplified by *B. putrificus*, are in reality to be regarded as bacteria characteristic of putrefactive conditions in the intestinal tract. They disappear largely when the food is changed to carbohydrate.

The second group, the obligate fermentative bacteria, grow best and are most numerous when carbohydrate forms a prominent part of the diet. These bacteria in virtue of the considerable amounts of lactic acid which they form under suitable conditions, are antagonistic to, and tend to replace, the obligate putrefactive (proteolytic) bacteria. *B. acidophilus* is the best known of this group. The third group, the facultative organisms, are those which accommodate, within limits, their metabolism now to a protein, now to a carbohydrate regimen. They are usually present in either class of food but are more numerous on the protein type of regimen, because they are less affected by the products of putrefaction,

than those of fermentation. *B. coli* and *B. proteus* are perhaps the best known of the facultative group.

We recognize, then, three well-defined types of bacterial activity in the intestinal tract, the putrefactive or proteolytic type, acting on the protein, the fermentative type acting by preference on carbohydrate, and the facultative type, which is by far the largest and best known, acting either on protein or carbohydrate.[1]

It is interesting and particularly important to recognize that the intestinal bacteria of normal nurslings are strictly fermentative. This is what one would expect, because the diet of the nursling is one well suited to encourage a fermentative flora, being composed of over 6 per cent. lactose and only about 1.5 per cent. protein. The reaction of a normal nursling's feces, furthermore, is strongly acid, due to the formation of lactic acid within the intestinal tract by this fermentative flora. It will be seen later on that this lactic acid, formed by the activity of fermentative organisms, is an important feature in keeping down putrefaction. In this connection it should be stated that the flora of normal nurslings contains few, if any, putrefactive organisms. As the child grows older and is placed on a cow's-milk diet, a change takes place in the intestinal flora: this change occurs less rapidly if the diet is strictly limited to modified milk, more rapidly if the diet is made up of unmodified milk or with the addition of protein. The change consists essentially in the replacement of the characteristic fermentative flora of the breast-fed baby by greater or lesser numbers of putrefactive and facultative bacteria. It is marked by the beginning dominance of the facultative bacteria which tend to persist throughout life.

The cause underlying this change is not difficult to define: the change in flora is largely attributable to the relative decrease in carbohydrate, associated with the increase of protein, two conditions favoring the development of a putrefactive or facultative flora.

It may be accepted as proved that the fermentative flora of the normal nursling is a valuable factor in protecting the host from invasion by foreign organisms, particularly of the proteolytic type. Consequently the lack of such a flora is to be regarded as a weakness in the normal defence against bacterial invasion of the intestinal tract. It has been

1. For a fuller discussion of these types, see Kendall, A. I. "Lactic Acid Bacteria: What They Are and What They Are Supposed to Do." Boston Med. and Surg. Jour., 1910, clxiii.

shown for example[2] that the intestinal flora in bacillary dysentery is essentially putrefactive in nature, at least in the more severe cases. It would appear logical and desirable, then, to attempt to reestablish and maintain the fermentative conditions at least in the intestinal tract of babies, and thus to encourage the reestablishment of the normal fermentative flora characteristic of such cases.

The question arises: How may this be accomplished? From what has been said it is evident that the increased administration of carbohydrate, and the restriction of protein will furnish the dietary conditions most favorable for the development of the appropriate organisms, and if the bacteria in question, the obligate fermentative bacteria, are present, and available in the intestinal canal, they may be brought up to their natural degree of activity. This process, however, takes a certain amount of time, and conditions may well arise in which the amount of time necessary to bring about this bacterial change will be prohibitive. For such cases, where time is a factor, and where it is desirable to populate the intestinal tract with useful types of fermentative organisms, the use of artificially prepared cultures of appropriate organisms is indicated, provided they can be obtained.

The observations presented in this paper are designed to show the feasibility of encouraging the growth of *B. acidophilus* by suitably modifying the food of the patient; if, however, acidophili are not present in the alimentary tracts of patients, it is apparent that they cannot be encouraged to grow even by the most careful dietary regulation. In such cases we deem it advisable, from the theoretical point of view, to introduce cultures of acidophili, provided they have been obtained from sources known to be normal and absolutely free from objectionable conditions.

The characteristics of this organism (*B. acidophilus*) have been described fully in a previous communication[3] and need not be repeated here.

Cultures were readily obtained from two different patients by feeding maltose or lactose in moderate amounts. The details of the feeding experiments appear below.

The patients were first put on a diet in which protein was in moderate excess, and the characteristic protein flora dominated, as is shown by the protocols. As the diet was gradually changed to one in which carbo-

2. Kendall, A. I.: Bacillary Dysentery, Boston Med. and Surg. Jour., 1911, clxiv, 288.

3. Kendall, A. I.: Jour. of Med. Research, 1910, N. S., xvii, 153.

hydrate predominated, there was a gradual restriction of the proteolytic flora, the more strictly proteolytic organisms diminished in numbers and the bacteria characteristic of the carbohydrate regimen, *B. bifidus* and *B. acidophilus,* gained the ascendency. These changes are of more than academic interest, for they indicate a possible method for controlling the proteolytic organisms, to a certain extent, at least, by dietary changes that are not only not harmful, but even under certain conditions beneficial to the host. While we are still quite in the dark concerning the absolute amount of importance to attribute to the presence of a more or less purely protein flora, the evidence is strongly in favor of the view that these organisms may not only be harmful themselves, but also that they may, and probably do, thrive in conditions suitable for the development of organisms like the typhoid or dysentery bacilli. On the other hand it is equally true that the conditions obtaining in the intestinal tract favorable for the continued development of the fermentative flora are inimical to the development of these pathogenic bacteria as well as for the putrefactive bacteria. Indeed, it appears to be a fact that the pathogenic organisms of the typhoid type, for example, are rather less resistant to the acids of the fermentative bacteria than are the more commonly met with putrefactive bacteria which occur from time to time in the intestinal tract.

It is not a matter of indifference which fermentative bacteria are encouraged to develop in the intestine; furthermore, certain organisms appear to elect the small intestine, others the large intestine. As a well-known example of the former, *B. bulgaricus* may be mentioned, while *B. acidophilus* is found most plentifully in the large intestine. Applying these principles clinically, it would appear that putrefactive conditions in the small intestine might be controlled more readily by an organism that generated lactic acid in that portion of the alimentary canal, and *B. bulgaricus* would be selected for this purpose, while *B. acidophilus* theoretically, at least, would be more promising for putrefactions of the large intestine.

We have shown that *B. acidophilus* was increased in numbers on the sugar diet, and this method of encouraging the growth of this organism would appear to be relatively simple. The time necessary to bring this increase in *B. acidophilus,* however, varies considerably and doubtless depends on the numbers and activity of the organisms of this type remaining when the carbohydrate regimen is instituted. There are cases in which it would be desirable, or even essential, to be able to introduce

large numbers of acidophili with the minimal expenditure of time, and we believe that artificial cultures of this organism are indicated. The problem arises: Is it possible to cultivate *B. acidophilus* in artificial media and still have it retain its desirable properties? Further studies on this point are needed before the question can be definitely decided.

It is evident from what has been stated that it is worth while to investigate whether the inhibitory action of *B. acidophilus* on certain harmful proteolytic organisms can be made use of therapeutically, and it is with this object in view that we have done some preparatory work on this subject. The first step in an inquiry of this kind is to obtain a strain of the acidophilus which has been shown to fulfil certain requirements, just as has been seen done with *B. bulgaricus*. This strain should be kept in pure culture ready for use according to the physician's demand.

After a series of investigations our interests centered on the following two cases which seemed to well illustrate how we obtained vigorous specimens of the *B. acidophilus* by carrying out suitable modifications of the diet according to the principles which we have described. These cases illustrate, furthermore, in a striking manner the alternations in the types of the fecal bacteria following the changes in diet. It is to be noted in studying the bacterial changes in these cases that *B. acidophilus*, like other bacteria, is selective of the kind of sugar that it prefers and thrives on, and that it is apparently encouraged to a greater degree of activity in a medium containing dextrose or maltose than any other sugars.

CASE REPORTS

CASE 1.—A boy, 6 months old, was being fed on a milk mixture containing a low protein, and for its sugar, lactose. The feces showed a moderate number of proteolytic organisms. On March 9 a high protein (3.50) was given and on March 13 the report of the feces was: Yellowish brown, with small curds; no mucus; slightly fetid odor. Bacteria: *B. coli*, *B. subtilis*, a few coccal forms; rather typical putrefactive feces both culturally and morphologically; practically no acidophili; many gelatin-liquefying forms. The food mixture was then changed to a low protein and the lactose replaced by a moderate amount of maltose—5 per cent. March 17 the report of the feces was: Yellow, with greenish color on the exposed parts; relatively homogeneous; odor not distinctive; *B. coli* and *B. subtilis* less in numbers; acidophili present in moderate numbers; a few bifid forms and a very small number of coccal forms appear; liquefying organisms greatly reduced in numbers and in activity. The maltose was then increased to 7 per cent. and the report on March 22 was: Yellow, granular and dry; *B. coli* and *B. subtilis* have almost disappeared; very few coccal forms persist; acidophilus and bifid forms increased. On March 27 the report was: Yellow, granular and relatively dry; bifid forms and acidophili present in considerable numbers; very few proteolytes; liquefying forms greatly diminished. On April 8 the report was: Small in amount, light color, with

greenish color on exposed surfaces. Proteolytic bacteria have almost disappeared. Culturally, very few liquefying forms are left; they are very inactive; acidophilus and bifid forms still dominate.

In this case a markedly putrefactive intestinal flora was gradually changed to a practically normal nursling's, and then to one markedly acidoduric by providing at first a protein diet and then carbohydrate. The acidophili were vigorous and were separated and kept in pure culture. They were used to coagulate milk but did not make an entirely satisfactory buttermilk. The reason for this appears to have been that the culture obtained at this time was less vigorous than those usually obtained under suitable conditions. This is in line with the well-known variations which different strains of the same organism not infrequently exhibit in artificial media.

CASE 2.—A boy 17 months old, was being fed on a rather excessive protein diet and on March 13 a report of the feces was as follows: Greenish, homogeneous with a few small curds which were very hard; odor suggestive of putrefaction in intestinal tract (indol odor marked); culturally, *B. coli* few in numbers; many subtiloid organisms; a few coccal forms were present; liquefying forms numerous and active culturally; no acidophili found. The protein part of the diet was then decreased and on March 17 the report was: Light yellow, with slightly sour odor; good feces morphologically; *B. coli* still present in small numbers; *B. subtilis* present although in fewer numbers; liquefying colonies still active and numerous; practically no bifid forms or acidophili. The diet was then made largely carbohydrate and on March 22 the report was: Light brown, smooth, homogeneous; *B. coli* very few in numbers; *B. subtilis* greatly reduced, both numerically and in activity. Bifid forms appear in moderate numbers, together with acidophili; feces changing from the putrefactive to the fermentative type. On March 27 the report was: Brown, smooth, homogeneous; moderately voluminous; odor slightly sour; no starch demonstrable microscopically; culturally, very few *B. coli*, few *B. subtilis*, little liquefaction, and few liquefying forms; bifid forms in moderate numbers; considerable numbers of acidophilic bacteria; feces distinctly fermentative in type. On April 5 the report was: Smooth, brown, homogeneous; slightly acid reaction and sour odor; culturally, very few proteolytes were found and those that were recovered showed but little liquefying activity; bifid forms more numerous, acidophili dominant; typical fermentative feces.

In this case a markedly putrefactive intestinal condition was gradually changed under the influence of a carbohydrate regimen to a typical fermentative one. The acidophili were vigorous and were isolated and kept in pure culture. When introduced into milk the resulting lactic acid coagulation was exceedingly satisfactory and so this strain has been retained for further investigation.

Successive transfers must now be made with this strain of the acidophilus to see if it retains its useful properties of antagonism to the putre-

factive conditions, which it has been shown to possess, or whether when used in milk it becomes acclimated and loses these properties. It is probable that it retains its strong lactic acid forming properties as does the *B. bulgaricus,* but if it does not it is possible that it may still be given therapeutically in a carbohydrate menstruum. If it can be given in this way it seems reasonable to suppose that the acidophilus will be superior to the bulgaricus in its power of inhibiting those putrefactive disturbances which are located below the ileocecal valve. It is here to be especially noted that while the activity of the bulgaricus grows less when it passes the ileocecal valve, that of the acidophilus increases, the latter always approaching in its downward descent its home, where it flourishes best, increases in number and vigor and produces most acid.

197 Commonwealth avenue.

DISCUSSION

DR. MORSE: I should like to make just one criticism, and that I think Dr. Rotch stated that the acid reaction of the stool was due to the sugar in the food. I think that in the normal stool the reaction depends on the relation between the fats and proteids in the food, and that the sugar has no effect.

DR. JACOBI: As far as this paper is concerned, I should like to say that I admire the industry displayed and its results. I began with a prejudice against the *Bacillus acidophilus* on account of its name. We have a prejudice against certain faces and certain names. I hope Dr. Rotch will find a better name for it. It is a long Latin name with a good sized Greek termination. This paper will do a great deal towards introducing the *B. acidophilus* into the literature, and I think Dr. Rotch should act as god-father and give it a better name.

As to the effect, I am delighted that there is something that can be given as a medicine to correct the mistakes of mothers, nurses, and particularly of doctors. If you insist upon feeding babies on an exclusive milk diet, you will have this condition. Then if you put in some *B. acidophilus* you can correct the disease you have been creating yourselves. It strikes me, therefore, that I have a right to repeat what I have so often said, Don't feed the milk in this way and then you won't have so many sour stools. Prevent them by adding what Dr. Rotch claims is the cure; that is, the carbohydrates. Do not give the milk without carbohydrates and you will prevent the necessity for using the *B. acidophilus.* We should prevent the condition more than we do by giving a food that is more digestible from the beginning, and I claim that all these scientific researches but confirm what I have done clinically for a half century. Do not feed milk without carbohydrates and you will be safe. What I have advised for so long is confirmed by all these modern researches such as those of Rotch and Escherich. The condition was produced by giving milk too plentifully and it could be remedied by substituting cane sugar or other carbohydrates such as cereals for the milk sugar. Escherich has come out several times with that teaching, finally, a few months before his death, which we all mourn, along the same line as Dr. Rotch has talked this morning. We should give the *Bulgarian* less chance and the *Acidophilus* more. In most cases we should not require the cure because we should prevent the condition.

DR. KNOX: I have been much interested in this paper of Dr. Rotch's, but I think that perhaps so far as the treatment of dysentery is concerned he takes a rather too optimistic view. The bacteria are located in the mucous membranes after the onset of the disease, and are in intimate association with the lymph and blood channels, so that I believe that while watching the reaction of the stools in the early stages of the infection might be helpful, I fear that in the care of ulcerative dysentery the change of reaction produced by feeding different forms of acid-producing organisms may not lead to a marked cessation of symptoms.

DR. DUNN: I should like to say in regard to Dr. Knox's remarks that at the Floating Hospital last summer some attempt was made to treat these patients by injections of sterilized dextrose solution into the blood. These cases are too few as yet to draw any definite conclusions from, but it was thought that there was some amelioration of the condition. It seems to me the great difficulty is that of getting a proper diagnostic basis. We have been using these various acid-producing bacilli in fermentative conditions without such a clear knowledge as we now have of the difference between fermentation and putrefaction. Probably we have been using the lactic acid bacilli at just the wrong time; just where it was contra-indicated. What we most need, I think, is a simple method of making the diagnosis. Dr. Kendall is now at work trying to devise some method of this sort which will serve as a guide.

DR. ROTCH: Dr. Knox is right in what he says about dysentery, and I think I referred to that in my paper—that we cannot reach the organisms after they have penetrated the mucosa. They do, however, produce toxins in the intestines, and we reduce the number of bacilli which are producing the toxins. We cannot overcome the damage already done, of course, but it seems to me rational to attempt to reduce the amount of toxins produced in this way.

In regard to Dr. Morse's remarks, it is possible that the acid in normal infants' stools may be produced by fats and proteids, but it is also well accepted that the carbohydrates and sugars do produce acid, and that changes in the diet bring about a change of the condition, and a change which is inimical to the putrefactive condition.

We have merely begun this study and it remains for the future to show what practical value there may be in the idea of changing the character of the attacking organism by changing the character of the food.

THE SURGICAL MANAGEMENT OF ACUTE ABSCESSES OF LYMPHATIC GLANDS IN INFANCY

THOMAS S. SOUTHWORTH, M.D.
NEW YORK

No surgical dictum has a broader application or more universal following than that which predicates that where pus exists it must be evacuated. That modern advances in the treatment of tuberculous or cold abscesses have led to some modification of its applicability in a limited field is but the exception which proves the rule. Almost as a corollary of the proposition that pus collections should be relieved by incision, there has grown up also a universal teaching that they should be laid open freely with a liberal incision.

Of course, if we assume that but one rule is to be applied to all purulent collections, no one will deny that the free incision insures the greatest safety in the largest number of cases. The futility of small incisions in cellulitis where the infection is diffuse and the process advancing, or in a deep-seated felon where necrosis of tissue threatens or has already taken place, has long been recognized. It is, however, worth considering whether this surgical canon has not been interpreted too broadly in extending its application to localized collections of pus, such as involve little of the danger associated with the rapidly spreading or necrotic types.

I have no desire or intention of trenching on the field of the general surgeon, or of entering on any further discussion of adult surgery, wherein my qualifications to advance an opinion might be questioned, but propose to confine myself to a group of cases belonging to the minor surgical affections of infancy, whose management falls naturally in the domain of the pediatrician, and where, in consequence, his experience over a period of years exceeds, as a rule, that of the general surgeon.

I refer to acute suppurative processes in the lymphatic glands in infancy. Here we are dealing with a suppuration beginning within the capsule of the gland, and rarely extending outside it, except in search of an exit to force its way to the surface or along some other line of least resistance. This latter tendency does not ordinarily produce a diffuse suppuration, but is a conservative process, planned by Nature solely to accomplish the spontaneous evacuation of the purulent collection. As

soon as such relief has been attained, the reparative forces of the body direct their energies to the task of restoring the tissues as nearly as possible to normal conditions.

When a lymphatic gland, one of whose important functions it is to arrest noxious bacteria brought to it by the afferent lymph-vessels, finds the task too great, suppuration ensues within the gland. Up to this point, although there is inflammatory enlargement of the gland, the gland remains distinct and movable, with no noticeable periadenitis. On the extension of the suppuration toward the periphery of the gland and progressive destruction of its parenchyma, a second line of defensive inflammation is established about the capsule, which limits the destructive process, except at the point which may be chosen as most suitable for spontaneous evacuation of the pus. At this stage, then, we have a periadenitis, the gland is less movable, and the presence of pus is practically certain.

From the foregoing it would seem possible to draw several lessons:

1. That in the common acute type of glandular suppuration in infancy and early childhood suppuration is not diffuse, but more or less limited by the line of the distended capsule of the gland.

2. That the infection having been rounded up and brought under control by the sacrifice of the parenchyma of the gland, Nature seeks as speedily as possible to evacuate the pus and detritus.

3. That our purpose, therefore, in incising such abscesses is not to check a destructive process by heroic measures, but to give just the requisite amount of aid to complete a conservative process.

4. That when this is accomplished, restitution of the surrounding tissues proceeds with the greatest rapidity.

It is probably the experience of others, as well as of myself, that incision of a gland which is only partially broken down into pus delays rather than hastens the period of healing. Once suppuration has begun in a lymph-gland its structure is apparently such that its destruction cannot be limited, but the entire gland must be broken down and thrown off. This process appears to proceed more rapidly before than after incision. Moreover, since complete breaking down of the gland is usually also accompanied by evidences of pointing, which indicates to us the most suitable point for incision, it is advisable, unless there are definite contraindications, to await distinct fluctuation before undertaking surgical relief.

In suppuration of the deeper-lying cervical glands, however, especially those lying beneath fascia, which reach the surface with difficulty, pointing, in the sense of increased redness, need not be awaited, but the site for incision chosen where distinct fluctuation is most superficial. If we follow Nature's wise lead in this particular, the required incision will be of less depth and will, as a rule, be more likely to avoid important structures.

It is, however, on the size of the necessary incision, and the nature of the drainage employed, that I wish to speak with particular emphasis. We have already seen that Nature only seeks an exit for the pus, and when this is suitably accomplished is ready to begin immediately the work of repair. It is understood, of course, that I am speaking only of acute processes, and not of tuberculous processes, which are subacute or chronic. The only justification for a large free incision is to secure drainage. Such free incisions in these acute abscesses of infancy, especially when made on an exposed region, such as the neck, are not only unnecessary from a surgical standpoint, but unnecessarily mutilating from a cosmetic standpoint.

As a rule, free incision and gauze packing go hand in hand. Necessary as they may be in diffuse suppurations, or where it is advisable both to prevent the reaccumulation of pus and to stimulate the tissues to throw off necrotic shreds and form healthy granulations, they are out of place in the glandular abscesses of infancy. The smallest incision which will allow of gentle expression of the pus, and the smallest tube drainage which will permit the continuous escape of the subsequent seropurulent discharge from the cavity, are all that is ever required.

Gauze packing, except in large wounds, dries in a few hours at the exit from the wound, and seals the exit. It then acts as a dam rather than a drain. Packing of the glandular abscess in infancy also prevents, rather than aids, the rapid contraction of the cavity, which is Nature's first step toward its obliteration. Free incision and attempted drainage by gauze are here illogical, the misapplication of a valuable principle where the indications for its use are not present. Cure, of course, follows free incision and gauze packing, but at the expense of more discomfort, slower healing, and a more disfiguring scar.

A long and not inconsiderable experience with all the usual ways of dealing with these rather common abscesses of infancy has led me to adopt the following plan:

As soon as the gland has softened so as to give distinct fluctuation, a site for the incision is sought, where the overlying tissues are thinnest, preferably near the lower border of the mass, and, if possible, in one of the natural folds of the skin, which may show as fine lines on the surface. An incision not exceeding five-sixteenths of an inch, and often shorter, is then made with a narrow, straight bistoury, through the skin and subcutaneous tissue, and, if pus is not immediately reached, further dissection and penetration is accomplished with a grooved director, until pus flows. Gentle pressure with occasional introduction of the director to dislodge flocculi is continued until the evacuation is complete.

The smallest drainage tube obtainable, not exceeding three-sixteenths of an inch in diameter, is fenestrated, slipped over a probe, and introduced to the bottom of the cavity. A bit of small catheter, from which a small segment has been cut longitudinally, in lieu of fenestration, serves well. A corkscrew motion often facilitates the introduction of either form of drain. If the incision proves rather small it may be stretched with dressing forceps or artery clamp, but not enlarged by cutting. The usual safety-pin of small size guards the drain, and a dry or moist dressing is applied.

This dressing is changed on the second day thereafter (forty-eight hours). Already the walls of the abscess cavity have contracted, and there are evidences that granulations have grown into the fenestræ of the tube. As a rule, only a little milky pus from the granulations can be expressed from the tract. In abscesses lying near the surface, the tube may often be removed entirely at this dressing, sufficient drainage being provided for by the temporary fistulous tract formed by the tube. In instances where the tube is found displaced by movement of the dressing, it is not necessary to replace it if the introduction of a sterile probe or director does not reveal retained pus. If, however, the abscess is one of a deep gland, and fascia has been penetrated to reach it, it is wiser to reintroduce the cleansed and shortened tube, to prevent retention by the narrow opening in the fascia.

At the second dressing on the fourth day, the tube may usually be dispensed with, and a dressing of ichthyol ointment — 10 to 20 per cent. — applied and employed for subsequent dressings until cicatrization is completed. This is not only more comfortable for the infant than the usual dry or moist dressing which soon adheres to the wound, but, while favoring drainage, also exerts its characteristic influence on surrounding induration of tissues or neighboring glands. Complete closure with a

minimal scar is found by the seventh day. I have but rarely been obliged to reopen the wound with a director after it is closed, and in these cases the character of the pus has indicated the breaking down of another gland and the escape of pus along the track of the first operation.

Under this simple but rational handling the rapid contraction of the abscess cavity and the restitution to normal has been surprising. The early removal of the tube I arrived at gradually, as the result of the successful outcome of cases where the tube was displaced accidentally by shifting of the dressings. The results of gauze drainage in my earlier cases, and in many others where I have made subsequent dressings on cases operated on by colleagues, do not compare with those from the use of the tube. There is almost invariably retention of discharges from sealing of the orifice by gauze. Packing not only prevents the rapid collapse and contraction of the cavity, but its use does not permit of so small an incision.

The lessened discomfort to the patient during the secondary dressings, while not a determining argument in favor of the procedure, is not without its appeal to the surgeon, and doubtless also to patient and friends. The minimal cicatrix is perhaps its strongest recommendation.

807 Madison Avenue.

COLON IRRIGATION: THE SHORT VERSUS THE LONG TUBE; A COMPARISON BASED ON TWO HUNDRED IRRIGATIONS

HENRY T. MACHELL, M.D. (Tor.)
Associate Professor Pediatrics, University of Toronto, Physician to the Hospital for Sick Children, Physician to the Infants' Home
TORONTO

For several years I have felt that in giving colon irrigations to children, the use of the small, short rectal nozzle is preferable to the rubber catheter or the flexible rectal tube. The short nozzle has seemed more agreeable to the patient and certainly is simpler for the physician, the mother or the nurse.

In a number of instances I have seen the tip of the catheter reappear at the anus when I had flattered myself it must be 10 or 12 inches up the colon. I have seen this occur to trained nurses, and to other physicians as well as myself. Therefore, I conclude, it could not have always been my technic which was at fault. Even if the usual directions as to (1) having the patient on the side; (2) having a volume of water of proper temperature ahead of the tip of the catheter; (3) gradual introduction; (4) the bag hung at proper height, etc., are observed, the nurse is fortunate, indeed, if she is not at times startled at the reappearance of the tip at the anus, or annoyed at the water not running out of the bag due to kinking of the catheter in the rectum.

Another objection to the catheter is that it must necessarily be introduced by a number of pushes or shoves, each of which irritates (it may be ever so slightly) the inferior hemorrhoidal nerves, and therefore gives some discomfort or sensation. Hence the longer and larger the tube the greater the number of pushes and consequently the greater number of uncomfortable sensations. A similar discomfort occurs during its withdrawal, though of course to a less degree.

When one bears in mind the fact that colon irrigation is commonly practiced for inflammatory conditions of the rectum and colon, the objection is worth bearing in mind. Another objection to the catheter, if it happen to be a stiff one, or if a heavy hand be guiding it, is a possible traumatism to the mucous membrane. Such a case I saw about a year ago.

The small nozzle, on the other hand, goes in almost of its own weight by one or two slight pushes — a minimum of anal sensation and irritation being produced. Another advantage is that it can be used by the mother, a neighbor, or an untrained nurse.

I have for a long time thought that the fewer the anal irritations the larger is the amount of fluid which can be injected and the greater the length of time it will be retained. But this theory is so much at variance with the practice advocated by recent English, German and American text-books, that I have hesitated to do little more than put my theory into practice as occasion offered.

With the view of trying to compare the short and long tube, I enlisted the aid of Dr. George Boyer, House Physician at the Hospital for Sick Children, Toronto, and Miss Bain and Miss Hill, senior nurses in charge of the baby wards. They were asked to see that the short and long tubes were used alternately, and that an accurate record be kept.

I have now the records of 200 consecutive irrigations done during the winter of 1909, an analysis of which I propose to give you.

The records were kept under the following headings:

Name and Date	Age in Months	Weight in Pounds	Disease, Acute or Chronic	Condition of Child—Weak, Fair Strong	Indication Blood Mucus Elimination	Last Stool Hours Ago	Amount Injected Before Return	Time Retained in Minutes	Nozzle Long or Short	Amount Finally Retained
1	2	3	4	5	6	7	8	9	10	11

2. The ages averaged 9½ months, the youngest being 3 months, the oldest 16 months.

3. The weight averaged 9 pounds 6 ounces, the lightest being 6 pounds 10 ounces, the heaviest 17 pounds 4 ounces.

4. There were 159 injections for acute diseases — mostly ileocolitis cases. There were forty-one injections for chronic diseases — mostly marasmus.

5. The condition was described as strong in twelve cases; weak in fifty-five cases and fair in 153 cases.

6. The indication was blood and mucus in 164 cases; elimination in thirty-four cases and not stated in two cases.

The time elapsed since the passage of last stool varied from fifteen minutes to twenty-four hours and seemed to have no bearing on either the amount injected before return or on "length of time retained."

Average time retained:

LONG.	SHORT.
31 returned at once.	31 at once.
22 retained up to 2 minutes.	28 up to 2 minutes.
15 retained 2 to 4 minutes.	18 2 to 4 minutes.

Thus the short tube has the advantage.

AVERAGE AMOUNT INJECTED BEFORE RETURN

Age			Weight		
Ac. Cases	Under 9½ mos.	L. 9.12 oz. S. 9.59	Ac. Cases	Under 9 lb. 6 oz	L. 9.52 oz. S. 11.37
	Over 9½ mos.	L. 15.00 S. 15.34		Over 9 lb. 6 oz.	L. 9.98 oz. S. 13.18
Ch. Cases	Under 9½ mos.	L. 13 oz. S. 15.71	Ch. Cases	Under 9 lb. 6 oz	L. 12.71 oz. S. 14.50
	Over 9½ mos.	L. 15.61 oz. S. 16.35		Over 9 lb. 6 oz.	L. 14.70 oz. S. 16.27

Amount Permanently Retained.—In only twenty-four injections was any permanently retained. In twenty-one of the twenty-four times it was given for the purpose of elimination. In these twenty-one the buttocks were pressed together for a few moments to insure retention. The amount retained varied from 2 to 6 ounces — with the L. catheter 4.7 ounces, and with the short nozzle 4.1 ounces.

As fluid was retained only three times, where pressure on the nates was not made, comparison is valueless.

I have not seen colon irrigation discussed on these lines heretofore, and I recognize some of the defects. I feel, however, that I have shown as far as 200 irrigations can be made to illustrate it:

1. That for the "amount injected" the short nozzle had the advantage, whether the cases were acute or chronic or whether the age or the weight was considered.

2. That it was retained for a longer time where the short nozzle was used.

3. That the "amount permanently retained" was larger where the short nozzle was used is not proved — no deductions can be drawn from so few injections.

That the fluid can be made to go up as far as the cecum with the short nozzle, one can readily prove by the use of the stethoscope as it is flowing up the bowel, but that the long tube ever gets even past the sigmoid is not so easily proved. That, however, is another question and is not within the scope of this paper.

If the short nozzle can be used with less discomfort and more ease, and, judging by the above figures, with better results, why use the more troublesome tube?

In practice I have not done so for fifteen years at least.

DISCUSSION

DR. JENNINGS: Dr. Yates, of Detroit, made some interesting investigations along this line. He showed that it was practically impossible to introduce a long tube into the colon. With the *x*-ray he made a series of experiments and showed that the tube could not be introduced above the sigmoid. It simply folded over and remained in the lower part of the bowel.

DR. JACOBI: The paper and the remarks by Dr. Jennings cover the case entirely, I believe. The Doctor might have gone a little further and given us the reasons why it is impossible, with rare exceptions, to put the long tube up into the colon. It is more than thirty years since I used to introduce a long, either flexible or stiff, tube into the colon. Whenever I use a tube of 16 or 18 inches, now and then, on examination of the abdomen I found the end of my long tube in the neighborhood just below the liver. I realized that the tube had not gone up the colon, but had raised the sigmoid flexure up to the lower border of the liver. It was not in the colon at all except a few inches below. That confirmed my idea on this subject. It is possible now and then to bring the long tube into the colon with adults but not with children. A flexible tube is apt to be bent upon itself. The sigmoid flexure begins a few inches above the anus and you cannot bring anything up but water. If you attempt it you simply lift up the sigmoid flexure. In newly-born babies, the sigmoid flexure is very long and often there are two sigmoid flexures. Those of us who have made a good many autopsies on very small children have realized that the lower part of the colon is longer comparatively in the baby than in the adult, and often we have found the end of the sigmoid flexure in the right side instead of in the left.* It is an anatomical impossibility to do anything with the long tube, and in thirty years I have not made an attempt to use it. I know I can do it better with the nozzle of the fountain syringe. In order to facilitate the operation it is better to raise the hips of the baby or child and have it lie a little toward the left rather than the right and the fluid will run in spontaneously.

DR. CHAPIN: I think this paper and discussion put on record will do good and add to the comfort of a great many poor babies. I have taught this for a good many years, without having performed the experiments that Dr. Machell has. You can get the same effect and with much more comfort with a short tube.

---

* That is why fifty years ago Huguier proposed to operate on babies for artificial anus in the right side, and not in the left; and why I could explain what I denominated congenital constipation, forty years ago, by the exclusive length of the sigmoid flexure.

DR. MACHELL: I would only say in closing that I got the idea from my own babies at home. One of my babies weighed two and a half pounds when born and only twelve and a half when a year old; he had ileocolitis most of that time, so that I had ample opportunity to do colon irrigations. Time and again in irrigating I found the tip of the nozzle protruding at the anus. The only conclusion I could come to was that the writers of text books advocating the long tube had not used it themselves in their own homes and their own babies as I was compelled to do.

DRAINAGE TUBE IN PLEURAL CAVITY (REMOVED WITH AID OF FLUOROSCOPIC SCREEN)

FRANCIS HUBER, M.D.
NEW YORK

In the *Medical Record* for Jan. 3, 1885, the writer reported a series of twenty-six cases, including two of his own, in which a drainage tube had been lost in the pleural cavity in empyema cases.

A few years ago one of the interns reported the loss of a drainage tube early one morning. At the regular visit a rib was resected and the tube readily recovered from the costodiaphragmatic sinus. Though the ordinary precautions are generally observed, the accident is of rather frequent occurrence. Dr. Hirsch, in a personal communication, stated that a surgeon in a large hospital met with the accident three times within a period of eighteen months. The following recent case is presented in detail as illustrative of the facility and certainty with which the lost tube may be recovered by a new and novel method.

Becky G., 2 years of age, was admitted to the Children's Service, Beth Israel Hospital, Sept. 9, 1909. The history in brief was as follows: About the latter part of April, at that time about 17 months old, she was operated on for empyema by simple incision and drainage. Two months later a rib was resected; since then she has been troubled with more or less gastro-intestinal disturbances. At the time of admission her general condition was reported to be good, though there was still a tendency to intestinal and gastric disorders. Some purulent nasal discharge existed, negative as to Klebs-Loeffler bacilli. Chest fairly well developed, expansion fair. Over the right side posteriorly below the angle of the scapula, a scar is seen, the result of former rib resection; also a small sinus leading into the pleural cavity. There is dulness at the base, somewhat distant breathing with diminished tactile and vocal fremitus probably due to a thickened pleura.

Left side not affected — no cardiac displacement.

September 22: General condition poor; patient is suffering from a severe exacerbation of enterocolitis, vomits a good deal; stools frequent and greenish. Temperature irregular, varying between normal and 102 F. Drainage good.

October 6: Condition better, temperature irregular, wound closed for nearly a week. Physical examination reveals a reaccumulation of the pleural effusion. Wound reopened and drainage tube inserted; considerable pus escaped. Temperature fell to normal and with the advent of cooler weather the diarrhea grew less and less with decided improvement in the general health.

October 24: When dressings were changed to-day the end only of drainage tube with safety-pin was found on the dressing, the rest. 2¼

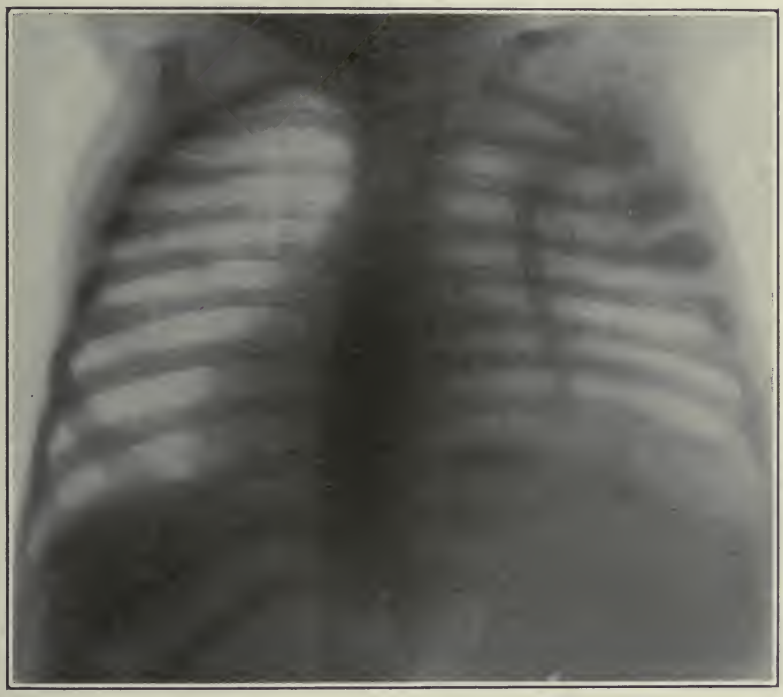


Plate I.—Lost tube distinctly visible.

inches in length (rubber catheter about 14 F.), had slipped into the pleural sac. (See *X*-Ray Plate I.)

October 25: Ninth rib resected, cavity carefully explored in various directions with finger and forceps without success.

October 27: Another *x*-ray taken (Plate II), the adjoining rib resected, and though a careful search was made with forceps and finger the tube was not found. As the child's condition was not good further

attempts were postponed for a few days. Under stimulation and forced feeding the child improved greatly.

November 3: The temperature having been normal for several days and the general state better, the child was again taken to the "*x*-ray" room in order to locate definitely the position of the tube by means of the fluoroscopic screen. I herewith extend sincere thanks to Dr. I. S. Hirsch, radiographist to the Beth Israel Hospital, for the radiographs and the suggestion to attempt the removal of the tube under the guidance

Plate II.—Shows changed position of lost tube. Below shows tube inserted for purpose of drainage and manner of securing tube with safety pin.

of the *x*-ray. To carry out the idea the child was placed face downward on the wooden table, the *x*-ray tube being hidden underneath out of sight of the child. Anesthesia was not required. Large curved throat forceps were then passed through the wound into the pleural cavity, and the fluoroscopic screen held in close contact with the posterior thoracic walls by Dr. H. M. Silver. The shadows of the forceps and the lost drain were

readily made out on the screen. It was a very simple procedure to open the jaws of the forceps, seize the rubber tube and accomplish its removal.

The subsequent course was uneventful. In a few days the patient was allowed out of bed. Dec. 28, 1909, the patient was discharged, physical condition excellent, wound completely healed, pulmonary expansion good. The slight scoliosis due to the empyema had been overcome by gentle massage of the thoracic walls and proper exercise.

Since the above was written the writer has had an opportunity to adopt the same method for the removal of a foreign body from the right bronchus.[1]

At the time the work was done and the article was published we were under the impression that the suggestion was original with Dr. Hirsch. Since then the writer has received a courteous note from Dr. Samuel Lile, of Lynchburg, Va., from which the following is quoted: "I am enclosing a reprint from the *Virginia Semi-Monthly* of Feb. 8, 1901, showing really where the idea originated. You will notice that my idea was correct, even if I did fail to carry it out with accuracy."

The article begins with the following: "The object of this paper is to call attention to the importance of the *x*-ray in locating foreign bodies in the air passages and esophagus, and suggest the possibility of removing them under the 'ray,' thus seeing every step of the operation, rather than probing for them with only the sense of touch as a guide." In the subsequent description of the examination of the patient under the *x*-ray, Dr. Lile says: "While looking at the nail the thought occurred to me, How easy it would be to pass a pair of forceps down inside the trachea into the tube, watch its every movement, even to grasping the nail and removing it."

To demonstrate the idea as nearly as possible, a board 5 feet long, 16 inches wide and 1 inch thick was procured, either end resting on a chair. With the Crooks tube underneath and the ray turned on, a pair of forceps passed between the patient reclining on the board and the fluoroscope were distinctly visible. Unfortunately, at the time of operation the room was heated to 85 F. by allowing steam to escape, thus interfering with the electrical apparatus and the successful carrying out of the idea. The foreign body was removed, however, after being located with a probe, by means of curved forceps passed into the left bronchus.

1. Reported in the Ann. Surg., Gynec. and Obst., May, 1910.

A READY METHOD OF CALCULATING MILK FORMULAS OF VARIOUS PERCENTAGES AND THE CALORIC VALUE OF THE SAME

L. EMMETT HOLT, M.D., LL.D.
NEW YORK

It seems hazardous at the present day to attempt to say anything new regarding methods of calculating milk percentages. The one which is here presented has, however, proved so easy of application and so easily grasped by medical students that its publication seems justifiable, especially since it is combined with a simple method of calculating the caloric value of the food when that is desired.

The more recent experience in infant feeding has shown the great practical advantages of using at times milk mixtures containing relatively low fat and high protein, and the need of some ready method of calculating such formulas with approximate accuracy has been felt. The use of top milks containing various percentages of fat made it easy to secure formulas containing higher fat than protein and also to increase the fat without raising the protein. The utility of such formulas has by no means ceased; but they need to be supplemented by others in which the percentage of fat is lower than that of the protein, and in which also the percentage of protein can readily change while the fat remains the same.

Starting with the belief that in practice it is unnecessary that the percentage of fat should ever be more than twice that of the protein, it has been found easy to construct a table by which a series of formulas can be obtained in which the fat may be as high as twice the protein, and as low as only a little more than one-fourth the protein, with all the variations between these extreme limits. The gradational differences given in the table have been found sufficient for practical work, but smaller gradations can readily be secured if desired.

The first step is to secure milks which contain different fat percentages: 7 per cent. of fat, 6 per cent., 5, 4, 3, 2 and 1 per cent. How this is done from one quart bottle of milk which has 4 per cent. of fat, and one which has 5 per cent. of fat is shown in the following table:

These figures are of course only approximate but repeated tests have shown the variations to be but slight from these averages.

Every ounce of 7 per cent. milk in a 20 ounce mixture will add one-twentieth of 7 per cent. or 0.35 per cent. of fat; every ounce of 6 per cent. milk will add 0.30 fat; every ounce of 5 per cent. milk will add 0.25 fat, etc.

Every ounce of each of these milks will also carry with it 0.175 per cent. of protein and 0.225 of sugar.

In the following table are shown the percentages of fat, sugar and protein of the different formulas which are obtained when one or more ounces of each of these milks (7, 6, 5, 4, etc.), are used in a 20 ounce mixture of food.

PERCENTAGES OF FAT, PROTEIN, AND SUGAR IN A 20-OUNCE MIXTURE

	Milk, oz.	Fat							Protein Per cent.	Sugar Per cent.
		A 7% Milk	B 6%	C 5%	D 4%	E 3%	F 2%	G 1%		
1.	1	0.35	0.30	0.25	0.20	0.15	0.10	0.05	0.175	0.225
2.	2	0.70	0.60	0.50	0.40	0.30	0.20	0.10	0.35	0.45
3.	3	1.05	0.90	0.75	0.60	0.45	0.30	0.15	0.50	0.65
4.	4	1.40	1.20	1.00	0.80	0.60	0.40	0.20	0.70	0.90
5.	5	1.75	1.50	1.25	1.00	0.75	0.50	0.25	0.85	1.10
6.	6	2.10	1.80	1.50	1.20	0.90	0.60	0.30	1.05	1.35
7.	7	2.45	2.10	1.75	1.40	1.05	0.70	0.35	1.20	1.55
8.	8	2.80	2.40	2.00	1.60	1.20	0.80	0.40	1.40	1.80
9.	9	3.05	2.70	2.25	1.80	1.35	0.90	0.45	1.60	2.00
10.	10	3.50	3.00	2.50	2.00	1.50	1.00	0.50	1.75	2.25
11.	11	3.80	3.30	2.75	2.20	1.65	1.10	0.55	1.90	2.45
12.	12	....	3.60	3.00	2.40	1.80	1.20	0.60	2.10	2.70
13.	13	....	3.90	3.25	2.60	1.95	1.30	0.65	2.25	2.90
14.	14	....	....	3.50	2.80	2.10	1.40	0.70	2.40	3.15
15.	15	....	....	....	3.00	2.25	1.50	0.75	2.60	3.35

Let us suppose the patient to be a young infant and 0.70 per cent. of protein to be proper. To secure this per cent. of protein, 4 ounces of milk in 20 ounces of food will be required. If this 4 ounces is of 7 per cent. milk the food will have 1.40 per cent. of fat; if it is 6 per cent. milk the food will have 1.20 fat; if 5 per cent. 1.00, etc. Let us assume the first mentioned, that 1.40 per cent. is desired. If we wish to raise both the fat and the protein proportionally the next increase would be to use 5 ounces of 7 per cent. milk in 20 ounces of food; later 6 ounces in 20; 7 ounces in 20, etc.

Assuming, however, that we wish to raise the protein above 0.70 but without increasing the fat, this can be done by using 1 ounce more of milk in 20, but of the series containing the next lower fat, e. g., 5 ounces of 6 per cent.; 6 ounces of 5 per cent.; 7 ounces of 4 per cent., and 9 ounces of 3 per cent., all give approximately the same fat while the protein is raised successively from 0.70 to 0.85, 1.05, 1.20 and 1.60 per cent. Roughly, instead of following the columns of the table vertically from above we follow them obliquely.

In calculating the sugar percentage it is necessary only to see how much must be added to that already in the milk to bring it up to the percentage desired, remembering that

1 ounce milk sugar by weight	in 20 ounce mixture	adds	5 per cent.
1 ounce milk sugar by volume	in 20 ounce mixture	adds about	3 per cent.
1 even tablespoonful	in 20 ounce mixture	adds	1.75 per cent.

When more than 20 ounces of food is to be made up one should add for 25 ounces one-quarter more of each ingredient; for 30 ounces one-half more; for 40 ounces twice as much, etc.

The next table gives the caloric value of 1 ounce of each of the percentage milks used in the table and also that of milk sugar, barley and other things one may desire to add to the food formula.

CALORIC VALUES

1 ounce 7 per cent. milk	27.5
1 ounce 6 per cent. milk	25.0
1 ounce 5 per cent. milk	22.5
1 ounce 4 per cent. milk	20.0
1 ounce 3 per cent. milk	17.5
1 ounce 2 per cent. milk	15.0
1 ounce 1 per cent. milk	12.5
1 ounce fat-free milk	10.0
1 ounce whey	10.0
1 ounce milk sugar by weight	116.0
1 ounce milk sugar by volume	72.0
1 even tablespoonful of milk sugar	44.0
1 ounce barley flour by weight	100.0
1 ounce barley water (1 tablespoonful to a pint)	2.0
1 ounce malt soup extract	80.0
1 ounce condensed milk	132.0
1 ounce olive oil by volume	245.0

In order to calculate the caloric value of the food quickly it is only necessary to note the number of ounces of the milk used in the formula, multiply this by the caloric value of 1 ounce, and add the caloric value of the sugar or barley used in the formula; e. g., for 40 ounces of the following formula:

There will be required			
Fat	3.50 per cent.	7 per cent. milk...	20 ounces
Sugar	6.00 per cent.	Sugar	2⅛ tablespoonfuls
Protein	1.75 per cent.	Lime water	2 ounces
Lime water	5.00 per cent.	Barley water	18 ounces
Barley water diluent			

Caloric value:—

Milk	20	× 27.5	=	555
Sugar	2⅛	× 44.	=	93
Barley water	18	× 2.	=	36
Total in food				684

While a knowledge of the caloric value of the food is not of great practical assistance in the problems of infant feeding it is sometimes useful in determining whether the food given is very much above or very much below the theoretical requirements.

14 West Fifty-fifth Street.

DISCUSSION

DR. BLACKADER: With a formula such as Dr. Holt has given us here, just what gain does he get in an average case?

DR. HOLT: By average I mean that these sixty-one children gained an average of 1 pound 10 ounces during their stay, the average stay being forty-seven days.

DR. CHURCHILL: I have been particularly interested in the hospital chart. General impressions are dangerous things to draw inferences from. But my impression is that these figures correspond to the results I have obtained in Chicago.

I should like to ask one or two questions. In the average gain, when the child went out, was that 1 pound 10 ounces above the weight when the child was admitted or above the bottom point in the hospital?

DR. HOLT: Above the bottom point in the hospital.

DR. CHURCHILL: I should also like to ask why Dr. Holt did not have more of the babies fed by partial breast feeding? Was it because he did not have more wet nurses? As to mortality rate, was it lower with the babies fed by partial breast feeding than was the general mortality rate? I am sure that breast feeding is a most valuable factor in the reduction of our mortality and think wet-nurses should be a part of the regular equipment of a hospital. We always keep two wet-nurses at the Children's Memorial Hospital, and it is astonishing how large a quantity or milk they will give after being in the hospital for a couple of weeks, with the stimulation of nursing. The maximum amount from one nurse I had was five quarts, by actual measurement. We never put the babies to the breast; the milk is pumped out. It is not fair to the wet nurse to let her run the risk of infection, e. g., from a syphilitic baby, with obscure or indefinite signs.

DR. RUHRÄH: Did the Doctor note any difference in the cases with gastro-intestinal disturbance, and those in which there was no such disturbance? I have always felt that those entering the hospital with gastro-intestinal disturbance did rather better than the others.

DR. FREEMAN: I think the way Dr. Holt has worked out these charts is very ingenious. The only disadvantage is that one has to carry his little booklet around with him. Most of us are getting down to much simpler dilutions of milk and not depending on such accurate percentages. It makes the subject easier for the general practitioner and medical student.

In reference to the application of the calories system to infant feeding confusion has arisen by trying to calculate calories by the metric system when we use ounces and drams in our formulas.

If the calories are estimated in drams and ounces, the caloric needs can be applied to any feeding in a few moments. Considering the caloric needs of an infant at birth as 50 calories per pound, and of a child at one year, 35 or 40; and the caloric value of an ounce of fat as 300, and an ounce of sugar or protein, 130, one may readily estimate the amount of fat or sugar or protein in any day's feeding and determine its caloric value. This method is easily applied in hospital rounds, and readily comprehended by medical students. Its value to my mind is rather in preventing the starvation of infants by too low a formulary or the overfeeding of infants that are disturbed by too much food, than for the purpose of modifying the feeding of any baby that is doing well.

DR. CHAPIN: I think it is very desirable for institutions to compare results as much as they can, but I question if the basis here advised will do; the terms are vague, and the personal equation comes in too strongly. When one is dealing with vague terms the matter of personal equation has to be considered. What one would call good another would consider fair or even bad. We must distinguish the cases in which there is gastro-intestinal irritation and those of pure marasmus. The marasmus patients will all die if kept in the hospital. A little breast milk is a great help in these cases.

DR. KOPLIK: I am pleased that Dr. Holt has shown that these infants do gain in American hospitals, because the young man who goes abroad comes back with the idea that we do not get any gain in our hospitals, especially as the Germans lay a great deal of stress on this gain. I consider the average gain shown here an excellent result.

DR. KNOX: I am glad Dr. Holt has said that he began his cases of malnutrition with mixtures derived from whole milk. The simple modifications from whole milk give gratifying gains. Except in very young babies we do not use cream mixtures.

DR. HOLT: There were six premature babies included in this group.

The reason we did not give more breast feeding was because we did not have the wet nurses.

The figures do not show that the majority of gains were due to wet nursing. Only twenty-seven of the patients got any wet nursing, and most of them but a few weeks. In no case was breast milk the sole food. Two-thirds of those classed as improved made their gain entirely on artificial feeding.

As to the influence of gastro-intestinal symptoms on prognosis, it seems to me that the outlook is worse and the difficulties of feeding greater when such symptoms are present.

DR. RUHRÄH: I would rather treat the ones that are vomiting in the long run.

DR. HOLT: The babies whose records are included in these tables had not been acutely ill, and in consequence, lost weight, but they were for the most part cases admitted for malnutrition in consequence of prolonged disturbances of digestion.

The gastric cases have generally been easiest to control, but the cases with intestinal symptoms seldom yield readily and most of the fatal cases were included in this group.

As to the value of the caloric method, so called, I do not think it helps us much. I have calculated the caloric values of the food used, more as a matter of general interest than anything else; but it has rarely been of practical assistance in our difficult problems. All of our children who do well have usually been getting from 125 to 150 calories per kilo. It seems to me we must rely on the percentage method as the best means of indicating exactly what we are giving our babies.

DR. CHAPIN: I am glad to hear such a good authority as Dr. Holt say what he has about the caloric method. My experience is that the more one uses it the less reliance he places on it.

DR. MORSE: It seems to me that Dr. Holt did not quite fairly state the question of caloric feeding. There is no question but that we should regulate our feeding on a percentage basis, but we can use our calories as a check to know if we are giving enough food in calories or not. I have found it a very useful check.

DR. COWIE: I do not agree with Dr. Holt as to the caloric method. I think we must use the percentage method as a basis, and use the caloric check if we are going to do our work in a scientific manner. When we find the children are not doing well and ask the intern if the child is getting sufficient calories we generally find that it is not, so I have constructed a chart to show the number of calories the child should have and the number furnished by the food. Since I have done this it has been surprising to see how the children have gained.

DR. GRIFFITH: I am much interested in this particular phase of the subject and I should like to maintain the position of the President and of Dr. Holt. I think the caloric method is a useful check, but after all the question to be decided is, What are sufficient calories for the individual child? It had been assumed that the matter was fixed and no one seemed ready to question this; but you may remember a recent contribution by a German investigator in which it seemed to be proved that an infant could gain on a much smaller number of calories than we had believed to be necessary. I have certainly seen children thriving and gaining weight on a number of calories decidedly less than the theoretical 100 per kilo of body weight. It appears to come to this, that the caloric need of one child is different from that of another, and until we know positively what is the absolute minimum we cannot use the caloric method with entire satisfaction. All this is on the supposition, too, that the caloric value of the food given is equally well utilized by the infants, and that the matter of the relative digestibility of the different constituents of the food is a matter of no consequence, and neither of these is in accord with the conditions which actually obtain.

DR. KERLEY: The amount of food required for a child can only be determined in one way, and that consists in feeding the child and finding out how much he requires in order that he may thrive. The activities of the child determine to a certain extent his caloric requirements, and as the activities vary very much, to determine a standard is most difficult. Further, the element of waste is an unknown quantity. Some children appear to digest all the food that is given them. Others only a part. Again there are children who require an enormous amount of food, perhaps twice the amount of a child of equal weight and vitality, and if they do not get it they fail to thrive or make their wants known in such energetic fashion that it is impossible to live with them unless this extra amount

of food is given. I recently had occasion to look over a large number of histories of children who had done well. I found that every child was getting more calories than he was entitled to according to the established standard. It was not at all unusual to find a finely thriving child get from 200 to 300 calories more than he was supposed to get. One child, I recollect, who was making a rapid gain and was the picture of health, was consuming twice the amount of calories supposed to be due him.

THE USE OF MALT SUGAR AND HIGH PERCENTAGES OF CASEIN IN INFANT FEEDING

JOHN LOVETT MORSE, A.M., M.D.
BOSTON

The differences in the digestibility and availability of human and cow's milk by infants, according to Finkelstein and Meyer,[1] are not due to qualitative differences in the constituents of the milk. Casein causes no disturbances of digestion. Fat and sugar have no pathologic action unless the intestinal functions have been injured. The fat and sugar of human milk can act in the same way if the injury to the intestine is severe enough. The action of the whey from human and from cow's milk is, however, different. A baby can digest the various food elements when they are in human whey but cannot when they are in the whey of cow's milk. Any other medium than human milk interferes with the functionating of the intestinal epithelium. They have, however, in spite of many experiments, been unable to find a better menstruum than the whey of cow's milk.

They believe that the diarrheal diseases of infancy originate in a functional weakness of the intestine, and that this functional weakness is kept up and increased by fermentation. This being so, the first step in treatment is to stop the fermentation and in this way give the intestine an opportunity to repair itself. This has been done in the past by cutting down the amount of food and by giving foods insusceptible to fermentation. This method is sufficient in many cases; in others, however, fermentation continues even when the caloric needs are not covered. In such cases the only recourse in the past has been human milk.

Fat, sugar and protein are all susceptible to decomposition. The medium in which they are contained, that is, the whey, may also play a part in the decomposition. Czerny and others have attributed the chief rôle in fermentation to fat, but Finkelstein and Meyer conclude from their experiments, in which they obtained the same results in these cases with diluted whole milk as they did with diluted skimmed milk and buttermilk, that the fermentation is not due to fat. They also found that the addition of freshly prepared casein to skimmed milk and to

1. Finkelstein and Meyer: Jahrb. f. Kinderh., 1910, lxxi, 525 and 683; Berl. klin. Wchnschr., 1910, lvii, 1165; München. med. Wchnschr., 1911, lviii, 340.

dilutions of whole milk, which babies with indigestion were taking, not only did not make the babies worse but apparently improved them. The thin, acid, green stools changed in a few days to typical light-colored and dry soap-stools. They conclude, therefore, that casein has an antifermentative action and is harmless. Milk-sugar must, therefore, by exclusion, be the cause of the fermentation. They found that the addition of milk-sugar to the food of babies whose diarrhea was controlled by the addition of casein, resulted in the recurrence of the abnormal stools. The long-continued diminution of the carbohydrates in the food also relieved the symptoms, even if the casein was not increased. They adduce as further evidence that the primary cause of fermentation lies in the sugars and not in the fats, the fact that when babies having fatty diarrhea were given the same amounts of casein and fat in various saline, sugar-free solutions instead of in the sugar-holding whey, the fatty diarrhea ceased. Milk diluted with water was, moreover, better borne than milk diluted with whey.

They sum up as follows: Sugar is the special and primary cause of fermentation. Neither normal nor abnormal acidification can take place without it. The fat is never involved primarily. It is injurious in that it causes an acid fermentation. The fermentation of the sugar is dependent on two main factors—first, the concentration of the whey, more or less work being thrown on the intestinal epithelium according to whether the concentration is more or less suitable for the intestine; second, the relative proportions of casein and sugar in the mixture. Here, therefore, as always in matters of nutrition, when considering the chemistry of the intestine, it must be remembered that it is impossible to judge of the action of one element alone, and that the final result depends on the relative proportions of the various organic and inorganic elements of the food.

They conclude, therefore, that the principles on which the preparation of a food to combat intestinal fermentation depend are: a diminution in the quantity of milk sugar, a diminution of the salts through dilution of the whey and an increase in the casein, with varying, and, under certain circumstances, not inconsiderable amounts of fat. After improvement has begun an easily assimilable and consequently little fermentable carbohydrate should be added. They consequently developed a food to meet these indications, to which they gave the name of "Eiweissmilch." This food is prepared as follows:

Heat one quart of whole milk to 100 F. Add four teaspoonfuls of essence of pepsin and stir. Let the mixture stand at 100 F. until the curd has formed. Put the mass in a linen cloth and strain off the whey from the curd. Remove

the curd from the linen cloth and press it through a rather fine sieve two or three times by means of a wooden mallet or spoon. Add one pint of water to the curd during this process. The mixture should now look like milk and the precipitate must be *very finely* divided. Add 1 pint of buttermilk to this mixture.

Finkelstein and Meyer use buttermilk in the preparation of this food for the following reasons: (1) because of the small amount of milk sugar which it contains; (2) to obtain the good effects of the lactic acid, and (3) because buttermilk can be kept for a long time.

The composition of this food is:

Fats	2.5 per cent.
Sugar	1.5 per cent.
Proteid	3.0 per cent.
Salts	0.5 per cent.

One quart of this milk contains about 370 calories.

They used this food in a great variety of conditions accompanied by diarrhea, such as dyspepsia, decomposition, intoxication and parenteral infections, and in their original paper claimed good results in all, but not in the new-born.

The general principles laid down by them for the use of this food in these conditions are as follows: A preliminary catharsis, if necessary, followed or not by an initial period of starvation and tea diet, as the case may be; small amounts of casein milk; larger amounts of casein milk; the addition of some carbohydrate other than milk-sugar or cane-sugar, preferably some dextrinized preparation of malt-sugar. They claim that the loose, green stools are quickly replaced by typical soap-stools and that the addition of malt-sugar does not cause a recurrence of the symptoms of fermentation. They call attention to the fact that on account of the low nutritive value of the food there is certain to be a loss of weight in the beginning of the treatment. This is followed by a stationary period, then, when the amount of food is increased and carbohydrates added, by an increase in weight. They found that babies could be kept on this food for months and continue to thrive.

Birk[2] obtained good results in the great majority of thirty cases of various sorts in which the patients were treated with casein milk. He believes that it is unquestionably of great service in many cases; that it is indicated not only in the acute toxicoses, but also in chronic disturbances of nutrition, in so far as there is in these cases an intolerance

2. Birk: Monatschr. f. Kinderh., 1910, ix, 140.

against fat; that is, in the cases in which buttermilk is ordinarily given. He found that as the result of the diminution of the sugar and the consequent diminution of the fermentation in the intestine the tolerance of the intestine toward fat increased.

Reuss and Sperk[3] also obtained favorable results in a small number of cases. They, however, attribute a part of the favorable results to the action of bacteria, believing that the administration of large amounts of casein diminishes fermentation and acts as the provocator of large amounts of alkaline intestinal secretion which neutralizes acid products and favors the development of bacteria antagonistic to fermentation. Welde[4] used it in sixty cases of various types and obtained satisfactory results. Nothmann[5] also obtained good results in a few cases, but Rommel[6] and Ibrahim[7] did not have as favorable results.

Braumüller[8] also used the casein milk in fourteen cases. He found, however, that in three of his cases serious symptoms developed when sugar was added to the mixture. In these cases the addition of even small amounts of sugar was enough to bring on a slow but uncontrollable decline, of which there had previously been no warning signs. A possible explanation is that the infant's powers of assimilation are greatly weakened and that it can produce only a limited amount of ferments. The large amounts of casein and fat in the casein milk demand so much of this power that the organism has but little strength left to produce the ferments which are needed to take care of the sugar. Pawlow has shown, moreover, that the sudden withdrawal of sugar produces an extinction of the secretion of the ferments concerned. Braumüller consequently advises delay in the addition of sugar in the severer cases and the substitution of oat starch for sugar in the beginning.

Finkelstein and Meyer[1] state in a later paper that this method of treatment is worthy of employment in the disturbances of nutrition in infants which are accompanied by diarrhea, no matter of what sort or severity. In their latest paper on "The Technique and Indications for Feeding with Eiweissmilch" they are evidently endeavoring to meet criticisms which have been made of their method of feeding. In this paper they still claim perfect results, and say that the bad results obtained by

3. Reuss and Sperk: Wien. klin. Wchnschr., 1910, xxiii, 9.
4. Welde: Therap. Monatsh., 1911, xxv, 83.
5. Nothmann: Jahrb. f. Kinderh., 1910, lxxii, 347.
6. Rommel: Jahrb. f. Kinderh., 1910, lxxii, 347.
7. Ibrahim: Jahrb. f. Kinderh., 1910, lxxii, 347.
8. Braumüller: München. med. Wchnschr., 1910, lvii, 2571.

others are due to imperfect technic or to a bad choice of cases. They now, however, warn especially against the continuance of under-feeding, advising the administration of as much as from 180 to 200 calories per kilo. They also warn against too long delay in the addition of carbohydrates, especially in feeble children, and against giving up treatment, withdrawing the carbohydrates and diminishing the quantity of food, if symptoms recur. They claim, too, that casein milk must not be combined with any other mixture, not even with human milk.

Leopold[9] has recently summed up the teaching of Finkelstein and his school as to the disturbances of nutrition caused by sugar in the food. These are of three sorts. It is, according to them, the chief cause of fermentation and consequently of diarrhea, plays an important part in the retention of water and, consequently, in the weight, and may cause an increase in the temperature, the so-called "sugar-fever."

He also investigated the action of the different forms of sugar, given by the mouth, in relation to the causation of diarrhea, to weight and to temperature. He studied chemically-pure lactose, saccharose, maltose and glucose, Soxhlet's Nährzucker and Löflund's Nährmaltose. The analyses of Soxhlet's Nährzucker and Löflund's Nährmaltose are as follows:

		Per cent.
Soxhlet's Nährzucker =	maltose	52.44
	dextrin	41.26
	sodium chlorid	2.00
Löflund's Nährmaltose =	maltose	40.00
	dextrin	60.00
	salts	.30

Milk sugar caused diarrhea the most easily, probably on account of its relatively slow absorbability, while the dextrin-maltose mixtures were comparatively well borne. The retention of water with the various sugars depended chiefly on whether the sugar caused diarrhea or not. In some cases, however, there was a retention of water in spite of the diarrhea. Fever occurred much less frequently with the dextrin-maltose mixtures than with the pure sugars. The tendency to increase in temperature stood in close relation to the action of the given sugar in causing diarrhea. Fever never occurred in patients whose stools remained normal, proving that there must be a lesion of the intestine before fever occurs. When sugar was added to different foods, fever occurred less often with foods poor in whey than with those rich in whey.

9. Leopold: Ztschr. f. Kinderh., 1910, i, 217.

He concludes that when a single dose of from 10 to 30 gm. of the different forms of sugar ordinarily used in feeding babies is given, the dextrin-maltose mixtures produce diarrhea and fever less easily than the pure sugars. Milk-sugar seems to be the one of the pure sugars which causes diarrhea and fever most easily. The condition of the intestine and the character of its contents, as well as the salts and sugar, are of significance in the etiology of "sugar fever." The temperature reaction occurs more frequently when the food is rich in whey than when it is poor in whey.

Having seen the rise and fall of many much-heralded foods and routine methods of feeding in the past, and being a firm believer in the adaptation of the food to the individual infant, I was not prepared to accept Finkelstein and Meyer's statements that this method of treatment is worthy of employment in all the disturbances of nutrition in infants which are accompanied by diarrhea, no matter of what sort or severity, and that all the bad results obtained by others are due to imperfect technic or to the bad choice of cases. Neither was I prepared to believe that all these disturbances occur independently of bacterial action, as the authors seem to imply. It did seem to me, however, that they had made out a very strong case against sugar as the etiologic factor in fermentation, and that the treatment of fermentative conditions with a food low in sugar and high in proteins was, therefore, a rational one. The substitution of the dextrin-maltose mixtures for lactose also seemed rational. It did not seem rational, on the other hand, to treat all cases in the same way, or to give all babies the same food without regard to their individual digestive capacities. The reasons given for the addition of buttermilk to the food, viz., its low salt content, its resistance to decomposition and its lactic acid content, did not seem very satisfactory, moreover, because the amount of salts in the precipitated casein is low, as it is in buttermilk, there is no reason for keeping the food a long time, and no evident reason why lactic acid should be of use in intestinal fermentation.

It seemed to me, however, that it would be possible to take advantage of the main principles of this method of treatment of the intestinal fermentative conditions and at the same time avoid the disadvantages of a routine food and the apparently superfluous buttermilk by applying them in the modification of milk by the percentage method. I was enabled to do this through the courtesy of the Walker-Gordon Laboratory. It was possible, by the use of cream containing a high percentage of fat, to reduce the amount of unprecipitated casein and whey proteins to a very

small percentage. Any percentage of proteins desired could then be added in the form of precipitated casein. The precipitated casein was prepared according to Finkelstein and Meyer's method, the casein from one quart of milk being made into an emulsion with sufficient water to make one pint. This emulsion, according to the analysis made at the Walker-Gordon Laboratory, contained less than 0.50 per cent. of sugar. It was thus possible to get mixtures containing 3 per cent., or even more, of fat, with less than 1 per cent. of milk-sugar. The "maltose" used in the mixtures contained 88 per cent. of carbohydrates, 57.1 per cent. being in the form of maltose and 30.9 per cent. in the form of dextrin. It contained no starch and had no diastatic action. Since the percentages of the different ingredients in the mixtures were known, it was always possible to calculate the number of calories taken.

This method of treatment was tried only in cases of intestinal disturbance associated with evidences of fermentation, and in which there was none or, at most, very little vomiting. Owing to the time of year at which this study was undertaken, only sixteen suitable cases were available. Eight of these cases must be excluded because of the short duration of the trial, the use of breast-milk in addition, or the presence of associated diseases, leaving only eight for analysis. The general impression derived from the few cases of parenteral infections was that this method of treatment was not very useful in these conditions. Eight cases is, of course, too small a number to justify any sweeping conclusions. They were carefully studied, however, and seem to show, or at any rate to illustrate, certain points fairly definitely. A detailed account of some of these cases or of parts of them will, therefore, be more instructive than any collective analysis.

CASE REPORTS

CASE 1.—A. O., 7 weeks old, was nursed for two weeks, after which she was fed on some milk mixture of unknown composition. She was brought to the Infants' Hospital by a woman who knew nothing as to the condition of her digestion or the character and number of her stools. She was in good general condition and the physical examination showed nothing abnormal. She was given a mixture containing 2 per cent. of fat, 7 per cent. of lactose, 0.75 per cent. of whey proteins and 0.25 per cent. of casein. She took this well and did not vomit, but had two large, loose, light-green stools daily.

March 23, two days after entrance, she was put on eight feedings of 75 c.c. each of a mixture containing 2 per cent. of fat, 2 per cent. of lactose and 2 per cent. of proteins, at least 1.80 per cent. of which was in the form of precipitated casein. The stool the next day was brownish-yellow, smooth and soft. This mixture gave only 60 c. per kilo, and the weight dropped from 60 to 80 gm. daily.

The food was increased March 26 to 80 c.c. at a feeding, and maltose enough added to raise the sugars to 5 per cent. She then got a little more than 80 C. per kilo and the loss of weight ceased. The stools at once became dark brown and pasty, but contained a large amount of fat in the form of soap.

Two per cent. more of maltose was added March 29, bringing the percentage of sugar to 7, giving 100 or more C. per kilo. On this she continued to have from one to three brown and pasty stools daily, and just about held her weight.

The maltose was changed to lactose April 7, the percentage of sugar being kept at 7. The color of the stools changed to yellowish-brown but no signs of fermentation developed The precipitated casein was replaced by ordinary milk proteins April 11 without any change in the general condition or stools (Chart 1).

In this instance the green color of the stools ceased at once when the percentage of lactose was reduced to 2 and that of the casein increased to 2. It did not recur when the percentage of sugar was increased to 7 by the addition of maltose. The tendency to fermentation was apparently relieved by this treatment, as the green color did not return when the maltose was replaced by lactose. It illustrates the loss of weight which takes place at first when the percentage of sugar is cut down. It is noticeable, however, that the baby did not gain when it was taking 100 or more calories per kilo.

CASE 2.—L. S., 4 months old, had been fed on a mixture containing 2.50 per cent. of fat, 6 per cent. of sugar and 1 per cent. of proteins and had done well until February 24, when she began to have four or five loose, green stools daily. She was admitted to the Infants' Hospital February 28. Physical examination showed nothing abnormal except the signs of slight malnutrition. She was given whey the first twenty-four hours and continued to have stools of the same character. March 1 she was given 2 teaspoonfuls of castor-oil and put on water for twenty-four hours.

March 2 she was put on a mixture containing 2 per cent. of fat, 2 per cent. of lactose and 2 per cent. of proteins, at least 1.80 per cent. of which was in the form of precipitated casein. The stools rapidly changed in character, that passed during the afternoon of March 3 being light yellowish-brown and smooth, with a little mucus but no curds. It contained no neutral fat or fatty acids, but a moderate amount of soap. She lost a little weight.

March 5 enough maltose was added to raise the percentage of sugar to 5. The stools then became somewhat more brown and were macroscopically perfectly digested. Two per cent. more of maltose was added March 8, and March 11 the percentage of fat was increased to 2.50. While taking this mixture she had from one to three smooth, dark-brown stools daily. They contained only a small amount of soap.

Lactose was substituted for maltose March 15, the percentage of sugar being kept at 7. The green stools did not recur after the change. The precipitated casein was replaced by ordinary milk proteins March 18. The stools then began to show an occasional casein curd but contained no fat, either macroscopically or microscopically. Gain in weight began at this time, whereas the weight had been stationary on the maltose and casein milk mixture of the same caloric value (Chart 2).

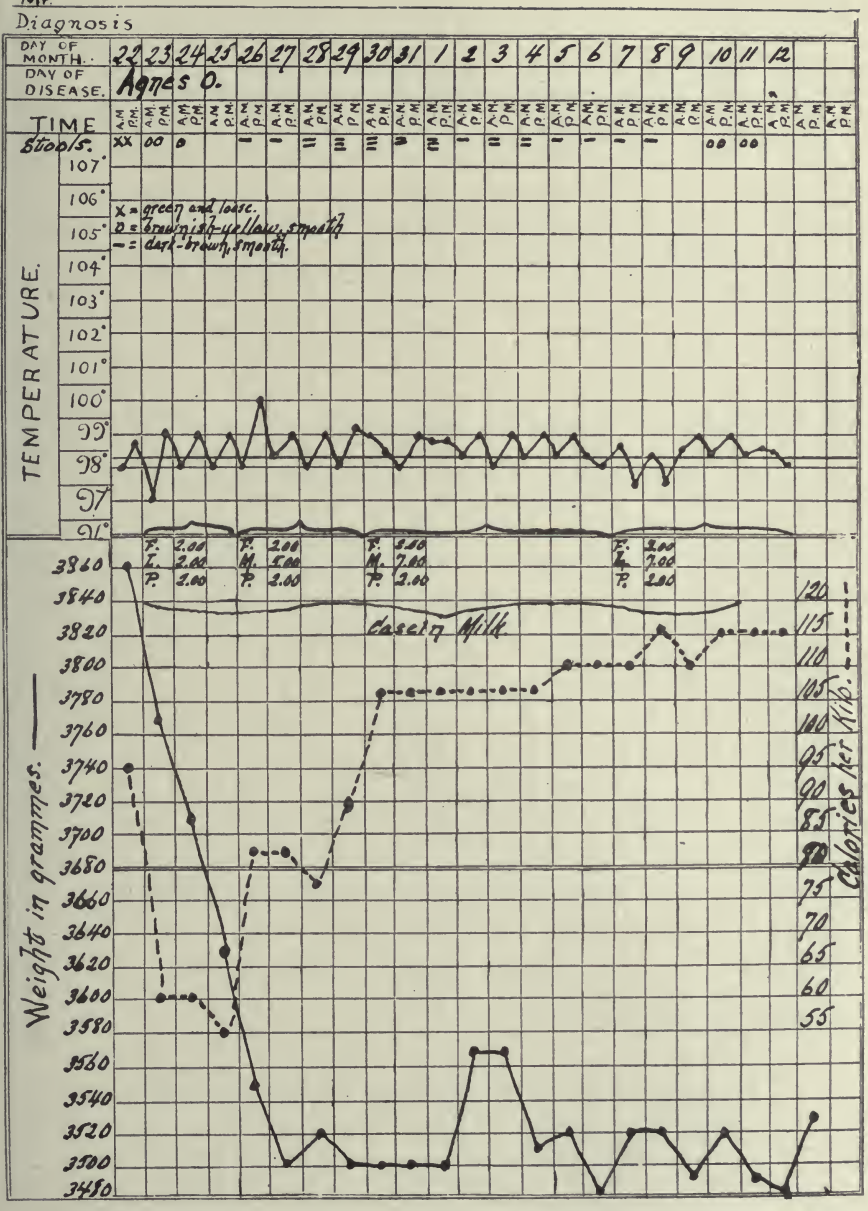


Chart 1.—Results of the use of malt sugar and high percentages of casein in Case 1.

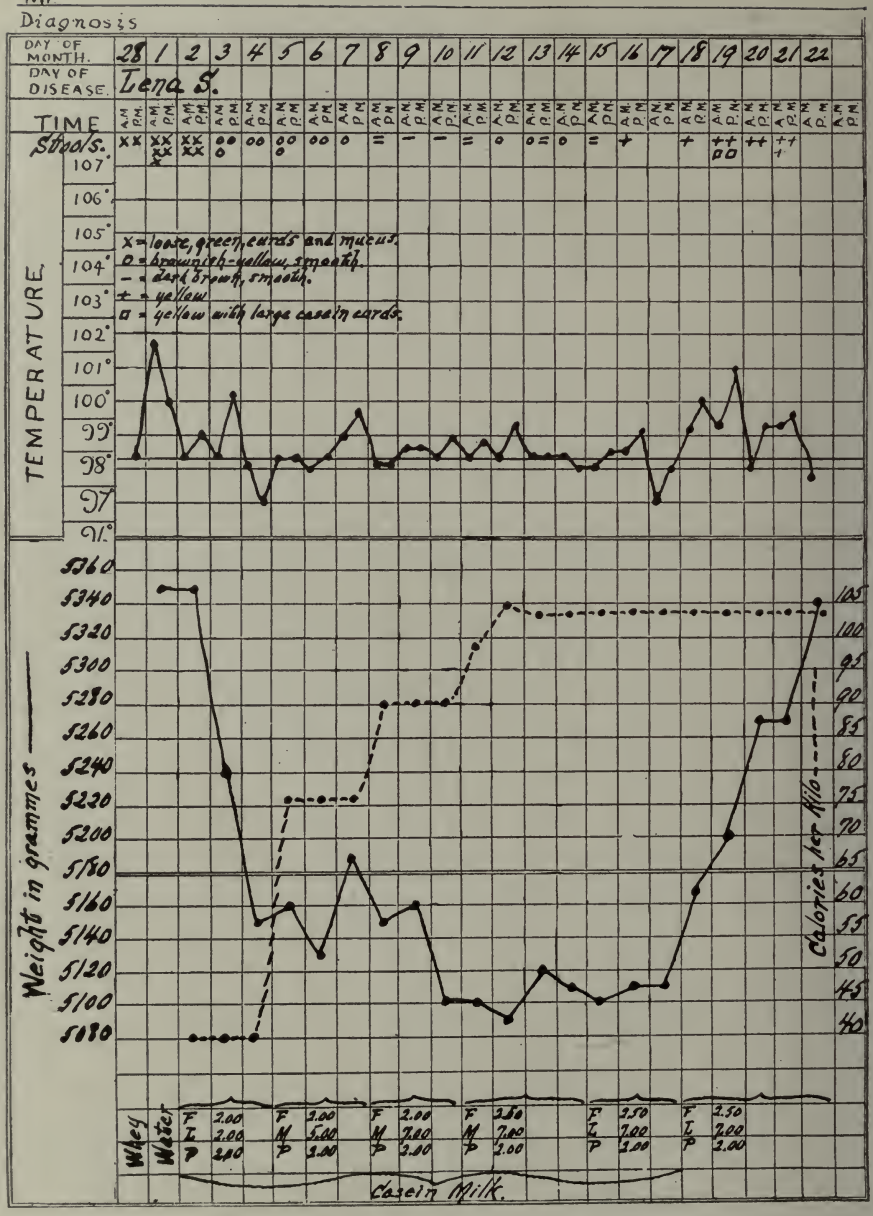


Chart 2.—Results of feeding malt sugar and high percentages of casein in Case 2.

In this instance also the green color of the stools ceased at once when the lactose was reduced to 2 per cent., and did not return when the percentage of sugar was increased to 7 by the addition of maltose. The tendency to fermentation was apparently relieved by the treatment, as the green color did not return when the maltose was replaced by lactose. The power of assimilating fat increased while on the maltose and casein milk mixture. It is noteworthy that casein curds appeared in the stools when ordinary milk proteins were substituted for the precipitated casein, suggesting that the casein is more easily digested after it has been precipitated and finely divided by rubbing through a sieve than when it has not been treated in this way.

CASE 3.—W. C., aged 5 months, was born one month before he was expected, but weighed 7½ pounds. He was never nursed, but was fed on a great variety of proprietary foods. He did well, nevertheless, for the first three months. Since then he had been constipated, but the stools had been green and undigested. He had lost weight steadily. He was small and poorly nourished, weighing on admission to the Infants' Hospital only 3,250 gm. The physical examination showed nothing abnormal except the signs of malnutrition. A skin tuberculin test was negative. The urine was normal.

He was given a teaspoonful of castor-oil at entrance and put on barley-water, containing 0.75 per cent. of starch, for twenty-four hours. He was then given a mixture containing 2 per cent. of fat, 2 per cent. of lactose and 2 per cent. of proteins, at least 1.80 per cent. of which was in the form of precipitated casein. He lost weight rapidly on this mixture and the stools continued to contain a few fine, soft curds. Microscopically, however, the stools contained but little fat, this being in the form of soap.

Four days later the percentage of sugar was increased to five by the addition of maltose. He continued on this mixture until his death, two weeks later. He lost weight more rapidly when the caloric value of his food was over 115 C. per kilo than when it was at about this level. The stools contained no fat, except that there were occasionally a few fine, soft curds (Chart 3).

In this instance there was but little evidence of fermentation. The stools were perfectly normal after beginning the mixture of maltose and precipitated casein and the fat was well utilized. He nevertheless failed steadily and died. He was willing to take all the food given him, but an increase in the caloric value of the food hastened rather than retarded the loss of weight (paradoxical reaction). In most instances, however, it was impossible to get the babies to take more than 120 calories per kilo; if they did the digestion was at once disturbed. Judging from my experience with these cases it would seem very difficult to give babies from 180 to 200 C. per kilo of "casein milk," as recommended by Finkelstein and Meyer.

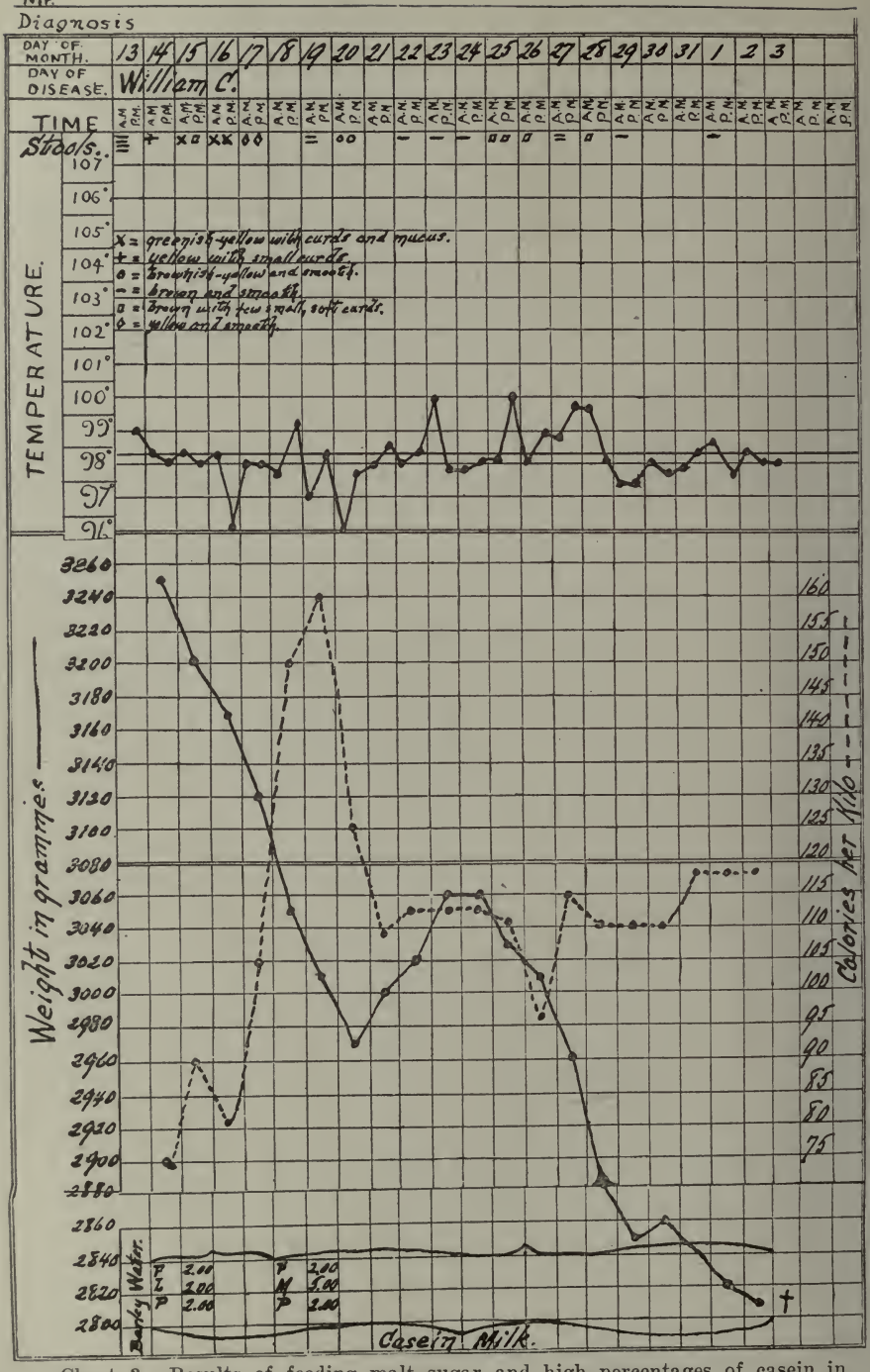


Chart 3.—Results of feeding malt sugar and high percentages of casein in Case 3.

CASE 4.—H. C., aged 4 months, had been fed for the last two months on a mixture containing 2.50 per cent. of fat, 6 per cent. of lactose and 1.50 per cent. of proteins. She had been having daily for some weeks five or six green or greenish-yellow stools, containing some curds. Physical examination showed nothing abnormal except the signs of slight malnutrition.

She was given on admission to the Infants' Hospital, April 6, a mixture containing 1 per cent. of fat, 7 per cent. of lactose, 0.90 per cent. of whey proteins and 0.25 per cent. of casein. While taking this mixture her stools were nearly normal. Thirty-six hours later it was changed, because of its low caloric value, to a mixture containing 2 per cent. of fat, 7 per cent. of lactose, 0.90 per cent. of whey proteins and 0.50 per cent. of casein. She immediately began to have numerous green or greenish-yellow, undigested stools.

Two days later she was given a mixture containing 2 per cent. of fat, 2 per cent. of lactose and 2 per cent. of proteins, at least 1.80 per cent. of which was in the form of precipitated casein. The green color of the stools ceased at once, but the small curds and mucus persisted.

Three days later the percentage of sugar was increased to 5 by the addition of maltose. The stools became normal after a few days, although, in spite of a sufficient intake of calories, there was a progressive loss of weight.

The mixture was then changed to one containing 3 per cent. of fat, 6 per cent. of lactose and 1.50 per cent. of ordinary milk proteins. The movements continued good and the baby began to gain in weight at once, although the caloric value of the food was no higher (Chart 4).

The good effect of this method of treatment on the fermentation was evident in this instance also, but the failure to gain in weight, although the number of calories was sufficient, was also evident.

In two instances it was impossible to increase the percentage of maltose above 5 without causing vomiting. The symptoms of fermentation were relieved in these cases as in the others, but the same difficulty was experienced in making the babies gain weight. This difficulty was encountered in almost every instance, although the number of calories given was theoretically sufficient. A number of them began to gain at once, moreover, after they were changed over to ordinary mixtures, although the number of calories taken was not increased. No difficulty was encountered in changing from the maltose and precipitated casein mixtures after the symptoms of fermentation were relieved, although the stools were sometimes temporarily not as well digested.

I feel certain from my study of these few cases that this method of treatment of intestinal disturbances associated with fermentation in infancy, by the withdrawal of lactose and by raising the percentage of casein, followed by the addition of dextrin-maltose, is a most valuable one. I am inclined to think that the finely divided precipitated casein, freed from the whey proteins, has some advantages over the natural

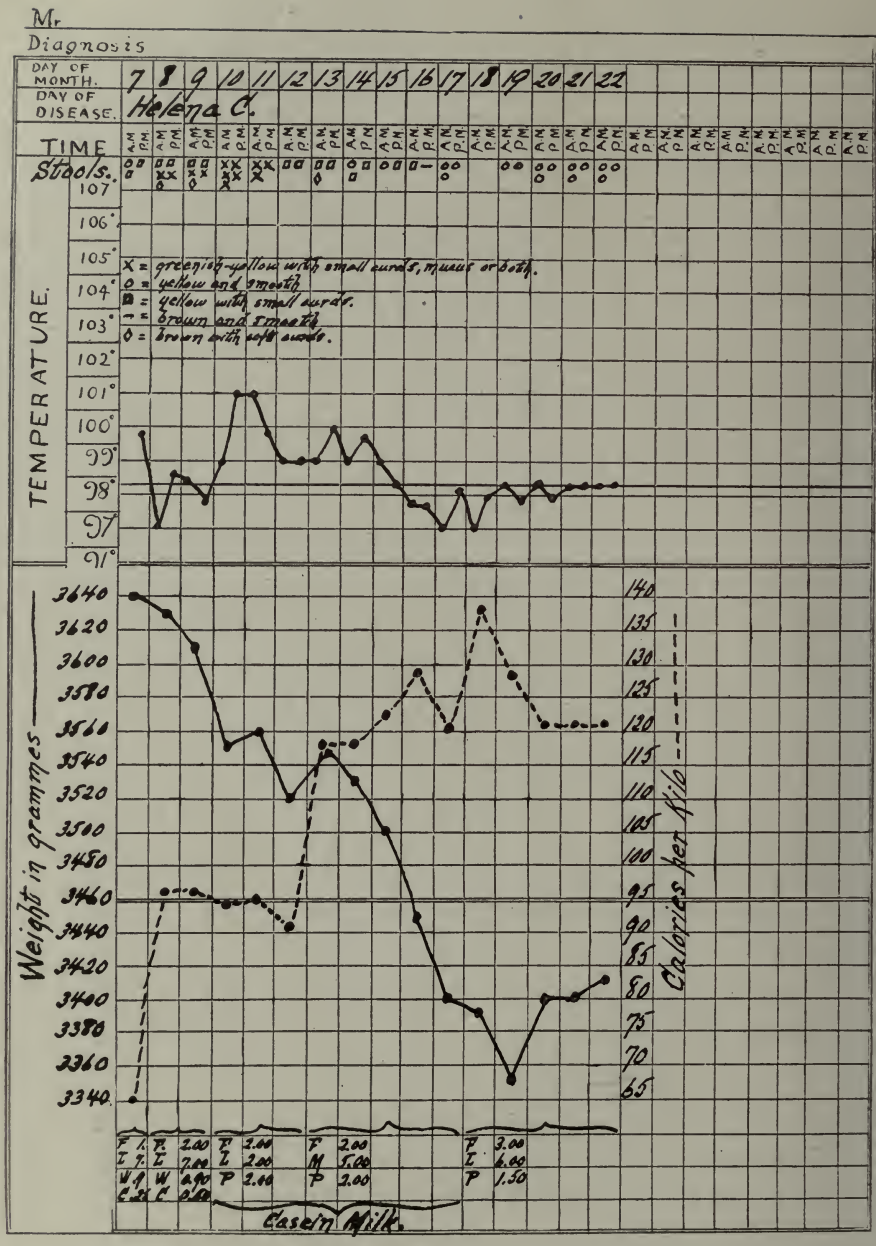


Chart 4.—Results of feeding malt sugar and high percentages of casein in Case 4.

milk proteins, but I am not sure of this point. I am also inclined to think that after the symptoms of fermentation are relieved babies do not thrive as well on these mixtures as on ordinary mixtures, and consequently believe that they should be discontinued as soon as these symptoms are relieved. I also believe, on account of the failure of babies to gain on these malt sugar and precipitated casein mixtures, even when given in amounts amply sufficient to cover the caloric needs, that this method of feeding is not one generally applicable.

70 Bay State Road.

ALBUMIN MILK AS CONTRASTED WITH OTHER MILK MIXTURES IN THE TREATMENT OF THE DIARRHEAS OF CHILDREN*

HENRY HEIMAN, M.D.
NEW YORK

Basing his treatment of the diarrheas of children on the supposition that the predominant etiologic factor is bacterial infection, it has been the aim of the pediatrist until recent time to provide a sterile food which at the same time is not a suitable culture medium. With this he usually combined the administration of drugs which were supposed to produce disinfection of the intestinal tract. The view that bacterial infection plays an important part in the diarrheas of children has gradually been losing ground in the last few years, chiefly due to the work of Czerny, Keller, Finkelstein, Meyer and Pfaundler. These investigators have shown that in a great majority of cases bacterial infection plays but a secondary rôle, and that the predominant factor is one or more constituents of the food which produces a disturbance in the metabolism. With the coming forward of this view it can be readily seen how the dietetic treatment must assume more and more importance. First of all, the proteids were held responsible, then the fats, and last the carbohydrates have been accused of being the offending agent. Starting with this supposition, that the carbohydrates are the active producers of fermentation in the intestines, Finkelstein and Meyer have recently advised the use of a food which they call "Eiweissmilch" or "albumin milk." The experience of Finkelstein and Meyer at the Kinderasyl in Berlin showed that an infant food which is adapted for the removal of intestinal fermentation must contain a minimum amount of carbohydrates and salts with a normal amount of casein and a variable amount of fat. They found that casein, when added to the diet of an infant suffering from intestinal fermentation, produces a rapid improvement in the stools.

Such a food is prepared as follows: A tablespoonful of Simon's essence of rennet (or two tablets of rennet) is added to 1 liter of milk, which is then placed in a water bath at 42 C. for one-half hour. It is then filtered slowly by gravity without any pressure for about one hour through cheese-

*From the Service of Dr. Koplik at the Mt. Sinai Hospital, New York City.

cloth. The coagulum is then washed twice in one-half liter of water through a very fine sieve and forced through by means of a wooden club. Then one-half liter of buttermilk is added. The chemical analysis of this food shows:

	Eiweiss Milk.	Cow's Milk.
Proteids	3.00	3.00
Fats	2.50	3.50
Carbohydrates	1.50	4.50
Ash	0.50	0.70

A liter of Eiweiss milk contains about 370 calories.[1]

Finkelstein and Meyer's results with this food in cases of diarrhea, including those of dyspepsia, decomposition, intoxication and parenteric infections, were strikingly brilliant. In most cases the diarrhea disappeared in the course of three days and the temperature became normal. It was found, however, that in the majority of cases there was a loss of weight during the continuance of exclusive feeding with Eiweiss milk. To overcome this loss, sugar in the form of Soxhlet's sugar, Liebig's extract or Loeflund's maltose was added in increasing quantities, as soon as the stools became formed. In most of the cases Eiweiss milk was used from eight to twelve weeks. In none of them was any deleterious effect demonstrated from this mode of feeding.

Finkelstein and Meyer's report on the striking results obtained with this food came out in the May and June numbers of the 1910 *Jahrbuch für Kinderheilkunde,* and did not reach us until July. Several weeks were consumed in overcoming technical difficulties in the preparation of the food, so that the greater half of the diarrhea period passed before it could be employed at the bedside. These remarks are made in anticipation of a possible criticism of the small number of cases reported on. In analyzing our tables it was unfortunately found that a considerable number had to be excluded for one reason or another as inconclusive, so that there remained only thirteen cases for the present report, which, had it not been promised for the present meeting, I would feel very reluctant to present at this time.

Eiweiss milk was administered to thirteen patients suffering from diarrhea for a length of time sufficient to determine its immediate effect on the general and local condition. I wish to make it clear that my aim was not to study the results of a prolonged use of the food, but its effect

1. Since the reading of this paper I have regularly added 1 grain of saccharin to each quart of albumin milk, finding the palatability of the food considerably increased by this addition.

during the first five days. This, to my mind, is the only fair test for the efficiency of any antidiarrheal dietetic or remedial agent. For the purpose of proper classification these cases were divided into moderate and severe. The moderate cases included those with only slight fever, mild general symptoms, and green stools varying from six to ten a day, containing mucus. The severe cases included those in which there was prostration, pyrexia and very many stools, eight to ten or more a day, green in color and occasionally blood-streaked. The latter class would come under the head of alimentary intoxication of Finkelstein. There were seven cases of the moderate type. Their ages were:

One	4½ months.	One	12 months.
Two	5 months.	One	15½ months.
One	7 months.	One	16 months.

All with the exception of two had previously been breast and bottle fed. Two were exclusively bottle fed. The duration of the disease previous to the admission to the hospital varied from five days to five weeks. The Eiweiss was given for a period varying from three days to twelve days. The effect of the administration of Eiweiss on the stools is shown in the following table:

	Prior to treatment.	Condition of stool after
1st case.	6 green stools.	Yellow after four days.
2d case.	Very many green stools.	Three green after eight days.
3d case.	5 green stools.	Two green after second day.
4th case.	10 green stools.	One green after second day.
5th case.	6 green stools.	Two green on third day.
6th case.	6 green stools.	No change.
7th case.	3 green stools.	One yellow after three days.

Of these three gained from 2 to 5 ounces and four lost from 2 to 5 ounces.

Maltose was added from the second to the tenth day, and in one case at once. All but one of these recovered.

There were six cases of the severe type — four were exclusively bottle fed; of the two others one had breast for three weeks and one for two months. The ages were:

One	2 months.	One	11 months.
One	5 months.	One	13 months.
One	8 months.	One	15 months.

The duration of the disease varied from four days to seven weeks. The Eiweiss was administered in these cases for a period varying from two to fifteen days. The effect of the stool is shown as follows:

	Prior to treatment.	Condition of stool after
1st case.	Very many bloody and green stools.	Green on third day.
2d case.	5 green stools.	No change.
3d case.	Frequent green stools.	Unchanged for eleven days.
4th case.	Many green stools.	Unchanged.
5th case.	8 green stools.	One, on third day, green.
6th case.	5 green stools.	Unchanged.

Three cases gained in weight and three cases lost; the average loss was 5 ounces and the maximum gain was 4 ounces. Maltose was added from the second to the sixth day. Three cases died and three recovered. The ages of the patients who died were 2 months, 11 months and 15 months. The ages of the three that recovered were 5 months, 8 months and 13 months.

For the purpose of comparing these results with those obtained by the use of other forms of diet, I collected twenty-four cases of diarrhea —

Seven of which received whey, barley, skimmed milk and milk sugar.

Four, skimmed milk, barley and milk sugar.

Five, whole milk, barley water and milk sugar.

Five, skimmed milk with sugar and water, and

Three, barley, rice water and milk sugar.

Of the seven cases that received whey, barley and skimmed milk, two were moderate; one of these had one stool on the third day, the other remained unchanged at the end of five days. The five severe cases showed no change in the condition in five days, although two ultimately recovered. The ages of the moderate type were 8 and 9 months, of the severe, 14 weeks, 7 months (recovered), 10 months, 11 months, 16 months (recovered).

Four received skimmed milk, barley and milk sugar. Two were moderate and two were severe.

Of the moderate cases, one on the fifth day had two stools and the other was unchanged.

Of the two severe, both of which died, there was no change within five days. The ages of the moderate cases were 4 months and 10 months, and the severe ones were 5 months and 22 months.

Of the five cases fed on the skimmed milk, milk sugar and water, three were moderate and two severe. Of the moderate cases one showed reduc-

tion from six green stools to three green stools on the fifth day, another one from five green to four yellow on the fourth day, and the third was unchanged. Of the two severe there was none on the fifth day in one case and unchanged in the other. One of these died, the other recovered. Of the moderate ones the ages were 2½ months, 7 months and 9 months. The ages of the severe were one 7 months (died) and the other 10 months (recovered).

Of the three cases that received barley or rice water, one was moderate and two severe. In the moderate case on the second day there was no stool, and of the severe, in one, there was a reduction from four to two green stools on the fourth day, the other was unchanged. The age of the moderate one was 17 months, and the ages of the two severe were 5 months and 16 months respectively, both of which died.

Taking these cases collectively, we find that there were twelve moderate and twelve severe cases. Of the moderate ones there was improvement within five days in six cases, and of the severe ones in two cases. Of the thirteen Eiweiss cases there were seven moderate and six severe cases. There was improvement in five of the seven moderate cases, and of the six severe cases there was improvement in two. We find, then, from this admittedly scant number of cases, from which I do not presume to draw any important conclusions, that whereas only 50 per cent. of the moderate cases fed with various milk mixtures showed improvement within five days, the percentage of improvement in similar cases in which Eiweiss milk was administered was 71.

In the severe cases of the ones fed on various milk mixtures the percentage of improvement was 16⅔, and in the Eiweiss cases the percentage of improvement was 33.

My impression, based on the clinical observation of the cases, is that this dietetic method of treatment deserves a further much more extended trial, which I hope I shall have an opportunity during the coming summer to carry out on a much larger series of cases. The present paper is merely offered as a preliminary study, showing at least the harmlessness of this therapeutic agent.

I wish to express my thanks to Drs. H. Emsheimer and G. Wetchler, interns at the Mt. Sinai Hospital, for their kind assistance.

DISCUSSION ON PAPERS OF DR. J. L. MORSE AND DR. HENRY HEIMAN

DR. KOPLIK: In justice to Finkelstein, we should first, if we are going to talk about his method, follow his instructions minutely. As soon as you begin to modify it, it is no longer Finkelstein's method. I agree with Dr. Morse that the disadvantage is that it is one food to fit all cases; it is too much of a routine.

His material is entirely different from that of Dr. Heiman. Most of his cases originate in his asylum and are under perfect control. As soon as the child has the least disturbance he begins his treatment. There are, then, a number of milder cases with the severe ones, and the statistics are drawn from both of these. The men who see his work do not consider when they return that he has very different material from ours. From the first minute the patients get ill he can treat them, which is very different from the conditions we have to deal with.

Finkelstein does not starve the babies too long and he maintains that his food can be given even when the baby is very sick; he rarely starves the baby over twelve hours.

Another point he makes is, and this is a very good one, that with older children he can get the same results, with other methods. The babies from earliest infancy up to three or four months are the cases he has his eye on.

DR. JACOBI: This method has several advantages: first, very little fat; second, very little milk sugar; third, more carbohydrates. That is just what we have done. Some of us have done this for fifty years and some for only a few years. The great principle in the treatment is, little fat, little milk sugar and more carbohydrates.

DR. ROTCH: I think that this method of Finkelstein's acts in much the same way as when putrefactive disturbances are combated by a carbohydrate regimen. In other words we can probably combat carbohydrated disturbances by means of a protein diet, and this may account in a measure for some of Finkelstein's success in treating this latter class of cases.

DR. FREEMAN: I think the advantage of the Finkelstein method is that it gives little fats and little sugar. While I have found it very good in children that were vomiting and had bowel trouble, children will not gain on it unless more sugar or fat is added.

DR. HOLT: It hardly seems to me that we can call Finkelstein's protein milk a low fat food. It contains, according to the milk from which it is made, from 2.5 to 3 per cent. of fat.

DR. MORSE: I hope I made it clear that I was not using the Finkelstein method. I merely adopted some of his suggestions and applied them.

It seems to me that Dr. Rotch has brought out a point in etiology that we are not in a position to settle at present. On the one side we have the chemical considerations and on the other the bacteriologic. We cannot with our present knowledge distinguish between them in many instances. It is probable that five years from now our ideas will be much more clear on the subject.

REQUISITE STANDARDS FOR RAW MATERIALS IN THE SUCCESSFUL SUBSTITUTE FEEDING OF INFANTS

HENRY L. COIT, M.D.
NEWARK, N. J.

Standards for the materials used in the artificial or substitute feeding of infants is a medical question of great importance and, as it relates to standards for milk and milk sugar, it has engaged the close attention of the writer for twenty-four years.

The problems growing out of the relations between the condition of raw food materials and success in their employment are, many of them, yet unsolved. Of these the clinical milk problems are perhaps the most insoluble and the profession is still left in a state of confusion and the authorities in disagreement.

It is my conviction that, with a proper unanimity of purpose, the leaders in the profession would soon leave the present diversity of opinion, the multiplicity of methods, the numberless rules for practice and the sharp controversial attitude of many in the background and the important subject of infant dietetics would be placed on a sound basis.

The universal standard for the food of the young infant is woman's milk and methods for artificial feeding should be determined with this ideal constantly in our minds. It has been too long the rule, when milk used for substitute feeding did not seem to agree after a brief trial or was accompanied by any disturbance, to transfer the infant to materials which represent neither the physiological nor chemical properties of woman's milk.

My experience would indicate that, if the milk is clean, the best way to obtain good results is to continue to work with milk even in the face of apparent failure; that when we follow correct principles and regard the derivatives of milk as a dietetic octave on which we may make as many combinations as a musician with his keyboard, and when we are broad enough not always to discard the thermic treatment of milk for refining purposes, then uniformly good results are sure to follow the use of milk.

Rules and recommended mixtures have long dominated the medical profession in infant feeding. The infant feeder should seek to know

fundamental principles rather than rules and make them his guide in determining has method.

General rules are unreliable because they cannot be adapted to the variations in individual infants, whereas, by guiding principles, we are enabled to make definite rules for each problem presented.

Principles formulated by the individual worker will lead him to such generalizations as the following: Never use any substance not isomeric with its counterpart in the infant's natural food.

Have a valid reason for the use of every element in the food combination.

Always determine the probable effect of each substance used on the nutrition of the infant.

Milk is the natural food for the feeding of mammals and since the milks of mammals have the same general composition and physical properties, the milk of one should be available for the nutrition of the young of the other.

The basis of an interchange of milks for the young of different species is a synthetic adjustment of the differences in composition yielding a milk approximately that of its own kind.

The lack of definite standards of quality and purity for milk and commercial milk sugar will be conceded by all. There is no uniformity in the character of these materials made use of in infant feeding and the lack of general knowledge with reference to their quality and purity explains the apparent failure and early abandonment of both of them so common by physicians.

Milk in its natural condition is free from foreign contamination and is practically sterile, and it should be the supreme effort to realize these conditions to infants fed artificially through clean milk or milk protected from foreign or dangerous contaminations.

Milk is generally accepted to mean one thing, whereas, milk must be considered as a general term. As many different kinds of materials are called milk and lactose (both far removed from ideal conditions of nascent purity) as there are different sources of supply or variations in the practice of cleanliness or varieties of animals yielding these products, or as there are changes caused by all possible sources of contamination — pathogenic, microscopic, macroscopic and chemical — or changes caused by the many kinds of ignorance and neglect in production, transportation or manufacture.

It will probably be true during our life time that if any member of the profession in any community succeeds in obtaining milk of the required clinical standards of purity and quality, he must struggle for several years with professional indifference before he may inaugurate methods and regulations which will yield what he requires and then he will need to pursue the fight eternally in order to keep what he has attained. The getting of clean milk is a problem requiring unremitting vigilance and a renewal of vigilance twice every twenty-four hours throughout the year.

In his struggle with problems in infant nutrition, it would be far more commendable if the physician would make the necessary sacrifice of time, comfort and money in a campaign to obtain the materials which would fulfil the highest standards of quality and purity than as now so quickly to abandon the logical milk for other substitutes which enable him only imperfectly to put the foundation under human life.

Milk of a suitable quality for successful substitute infant feeding will never be obtained until physicians generally, and pediatricians in particular, realize that they must expend on it more mental energy than is required for the solution of any other problem.

After twenty-four years of effort, I believe it is hopeless to expect to bring milk up to a grade of clinical efficiency by stimulating officers of the law or milk concerns or by demands through the press. The public has no adequate knowledge of this subject, neither has the rank and file of the profession. If milk fit to use for infants or for the sick is ever obtained, we must do the work necessary for its attainment ourselves. It is my opinion that if four physicians in any community would bend their earnest efforts to obtaining clinically clean milk, the milk millenium for that community would arrive in five years.

The fixing of definite standards of quality and purity should claim our earnest attention. What these standards shall be remains for the combined judgment of men who have had experience and are thus qualified to determine the range of variations in milk and other materials employed in infant dietetics.

It is quite as essential that standards for raw milk and milk sugar should be fixed for their clinical values as that standards should be required by law in order to market them.

During the past twenty years attempts have been made to standardize many products such as remedial agents, therapeutic serums, antitoxins, chemicals and galenical drugs, and while milk and its chief by-product,

milk sugar, should both be standardized as to purity and quality, this has not thus far been accomplished.

We are just beginning to realize the necessity for definite knowledge of our food materials in order to determine their energy equivalents. We have learned how to express the food in percentages and to measure it on a calorimetric basis but we have not yet simplified these scientific procedures or made them as precise as they should be because we have not fixed uniform standards for the raw materials employed.

We have passed the empirical stage of infant feeding and what we most need for further progress is food material which represents something exact in quality and purity, and there is no way to properly estimate our results without first knowing what the materials represent in food values and freedom from foreign matter, bacterial and toxic contamination or impurities inimical to infant nutrition.

Nutritive efficiency in milk depends quite as much on freshness and freedom from foreign contaminations as it does on chemical balance or food values. This is abundantly proved by the feeding of infants with contaminated milk, which so often misses the mark, even though it is accurately adjusted and also by the direct and successful suckling of goats by human infants, without percentage adjustment. If the claim that quality and purity are important factors in the successful use of milk, then a reference to my own personal experience in artificial feeding would not be presumptuous.

I have had the care of a large number of feeding cases during the past twenty years and have not felt called on to use a patented baby food during this entire period. Without having any prejudice against these substitutes for milk, I have not once been obliged to resort to dextrin, maltose, condensed milk, malt soup, casein milk, buttermilk or dextrin gruels except as starch was designedly added to milk after seven or eight months, and I attribute my results, which have been most gratifying, in a large measure to my ability to obtain for thousands of private and hospital cases alike, a very clean and fresh milk.

A system under strict medical control whereby clean and uniform milk may be obtained for infant feeding was inaugurated in the United States in 1890 by the Medical Milk Commission.

Through this agency the possibility of obtaining in many cities a clean, raw, clinically safe milk was demonstrated. The Medical Milk Commission has been called the backbone of the pure milk movement. Dairies under its supervision have served as models for much educational

work by the government and one of its most far-reaching results has been its influence on municipal reform for the control of the general milk-supply of large cities. The Medical Milk Commissions have done much to establish standards of quality and purity.

The original Medical Milk Commission adopted the following clinical requirements for the "certified milk" produced under its control and supervision:

First: An absence of large numbers of microorganisms and the entire freedom of the milk from the pathogenic varieties.

Second: Unvarying resistance to early fermentative changes in the milk, so that it may be kept under ordinary conditions without extraordinary care.

Third: A uniform nutritive value of known chemical composition and a constant relation between the percentage of the fats, proteins and carbohydrate.

When the Medical Milk Commissions in the United States were federated, an attempt was made to harmonize the requirements of all commissions and officially to fix standards for the milk produced under their control. Each year these standards have been revised and at the present they represent the results of four lines of scientific control touching the hygienic, biological, veterinary and medical aspects of milk production designed for clinical purposes.

The standards now require the highest type of dairy husbandry, perfect health in the animals, the use of every known precaution to exclude bovine tuberculosis and the practice of dairy hygiene with reference to buildings, premises, utensils and the animals.

The chemical standards require the milk to be free from preservatives, to contain a percentage of fats, in so-called 4 per cent. milk, ranging between 3.5 and 4.5 per cent., or in 5 per cent. milk, ranging between 4.5 and 5.5 per cent., with protein content between 3 and 4 per cent. The test for heated milk is also required.

The bacteriological standards are also fixed with the laboratory technic prescribed to determine the bacterial content of given samples of milk. The maximum average numerical limit has been fixed at 10,000 per cubic centimeter, with at least a biweekly planting throughout the year.

A standard of safety is also prescribed through medical supervision of all the employees on the dairy as well as of the transfer agents, with a continual guarantee of their health and personal hygiene.

These standards are far from being comprehensive and they should be augmented by requirements on the chemical nature of the fats, and requirements on the chemical nature of the protein content of the milk. While a limit of 10,000 bacteria per cubic centimeter is perhaps the best we can hope to attain in the present state of our knowledge of dairy hygiene, yet for clinical efficiency milk should be nearly sterile and we should aim to accomplish this, which is not impossible.

One dairy making certified milk has been able to deliver sterile cow's milk through clean methods several times during the year with an average bacterial count of 400 per cubic centimeter.

There should be a standard of temperature and a standard of freshness which should require a temperature acquired within one hour of milking of 48 F., and maintained within 5 degrees of this point until used. Milk should be not over fifteen hours old when received and not over forty hours old when consumed.

Of the by-products of milk, the most important is milk sugar or lactose, the logical carbohydrate. Many tons of this sugar are employed annually in feeding the American baby. It is far from being an ideal food. It is manufactured in forty-two sugar refineries in the United States. Twenty-five years ago it was made in only one. These refineries are controlled by one holding company. The milk from which the sugar is obtained is of a grade which probably could not be otherwise marketed for food. It is bought for an astonishingly low price and hauled to the refinery where many products are made from it. The first and most important commercially is sizing for wall paper, made from the casein.

The end product is the milk serum or whey which, contaminated with factory dirt and toxins from the myriads of bacteria in the milk, is finally reduced to a semicrystalline magma of crude, impure sugar. This coarse sugar is reduced again by heat and crystallized on cobs. It is of a light brown color and when ground in a mill constitutes the sugar of milk of the market.

Three years ago I succeeded in persuading the National Milk Sugar Company to refine this market sugar by two or more extra crystallizations in order to remove the gross impurities and the color, and to attenuate the bacterial toxins which the general chemist of the concern admitted were present. I believe that many of the difficulties of bottle feeding are due to ordinary milk sugar. This belief is borne out by results of using a milk sugar of this extra refined grade with marked absence of clinical difficulties attending the use of ordinary sugar of milk.

The toxins of some of the milk bacteria are heat resistant, notably that of the *Enteritidus* of Gärttner and the *Bacillus paratyphosis*, which is responsible for ordinary ptomain poisoning. According to Rosenau the toxins of some of the colon group are also heat resistant and probably account for some of the vomiting, the depression in infants and also for the diuretic effects of milk sugar. Sugar of milk for infant feeding should fulfil higher standards than is now required by the pharmacopeia, which simply calls for freedom from copper, lead, arsenic and other gross contaminations from the vessels used in its manufacture.

Milk sugar for clinical purposes should be made from the whey of fresh and high grade milk.

It seems to me desirable that some representative society of physicians, trained in pediatric practice, should determine the proper clinical standards for milk and milk products. Such society should not only fix these standards but from time to time should elevate them with the acquisition of more advanced knowledge.

277 Mount Prospect Avenue.

FURTHER OBSERVATIONS OF THE ACID CONTROL OF THE PYLORUS IN INFANTS*

DAVID MURRAY COWIE, M.D., AND WILLIAM LYON, M.D.
ANN ARBOR

In a former paper[1] we recorded two experiments on the acid control of the pylorus in infants. We have since extended and verified these results and present them herewith, together with a partial description of the first experiments.

HISTORICAL NOTE

The explanation of the opening and closing of the pylorus was not fully made until Pawlow and Cannon's work was done. Not long after Beaumont's experiments in 1832 it is true that Hirsch, by means of a duodenal fistula in a dog, came to the conclusion that acid on the duodenal side caused the pylorus to close, but he abandoned his idea in favor of von Mering's observations, made about the same time, that the closure of the pylorus was due to the bulk of liquid or food in the duodenum. In his experiments von Mering introduces milk into the duodenum. The observation that the mechanical effect of inflating a small rubber balloon in the duodenum causes the pylorus to contract and its rhythmic movements to cease, seemed to lend support to von Mering's theory.

It was left for Pawlow and Cannon, however, to clear up these discrepancies and make full explanation of the phenomena observed by Hirsch and von Mering. Pawlow demonstrated that milk or neutral fat in the duodenum, whether in small or large bulk, excites the duodenal closing reflex and keeps the pylorus closed until the neutral fat has become saponified or until it has passed on into a lower segment of the intestine. He also showed that acid on the duodenal side closed the pylorus. Later Cannon demonstrated that acid in the stomach opens the pylorus and that the differential escape of carbohydrates and proteins from the stomach is due to their respective stimulating and combining property for hydrochloric acid. Hence the observations of Hirsch and von Mering were correct, but their explanations were entirely faulty.

---

*From the Pediatric Clinic, University of Michigan.

1. Arch Pediat., February, 1911.

AUTHORS' EXPERIMENTS

The experiments which resulted in the above observations were performed on dogs and cats. Of the various methods used Cannon's is probably ideal, as it removed practically all abnormal conditions. In conducting our experiments we have been aware of the arguments against the accuracy of the method of tubing the stomach and we have not lost sight of the possible effect of the preantral sphincter on our results. The small size and the elasticity of the infant's stomach better adapt it for such observations than the adult stomach, and for these reasons we believe that the method we used, properly controlled, fully demonstrates the point at issue.

Method.—We selected babies who had proved their indifference to the passage of the tube. That is, they had become accustomed to the tube and retained it with perfect ease for any period desired. They would often sleep throughout an experiment, excepting for the brief interval of passing the tube. We found No. 14 (English) soft rubber catheter connected by a piece of glass tubing with a rubber tube and small bulb the most satisfactory apparatus for our work. As we had not investigated the effect of posture on the rate of stomach evacuation we had the position of the infant constant; that is, lying on the left side.

Control Test Meal.—Skim-milk, diluted one-half with water, was employed as a suitable test meal for these investigations. The meal usually contained a fraction of 1 per cent. of fat and proved more convenient to work with than milk containing a higher fat per cent., and this removed from discussion the possible effect of fat on the pyloric reflex. A definite amount was delivered to the stomach through a tube and allowed to remain a definite time. It was then recovered by expression and syphonage as described below.

Acid Meal.—This meal was prepared by treating skim-milk with dilute hydrochloric acid (10 per cent. solution) until the acidity desired was obtained. The food was then kept at body temperature for an hour to insure complete combination of the acid with the protein. It was then retested and treated, if necessary, to insure the acid value as it entered the stomach.

Basic Meal.—The basic calcium casein meal was prepared by adding the requisite amount of lime water to the skim-milk to render it faintly but distinctly alkaline to phenophthalein. The balance of the dilution was then made up with water so that, as with the control and acid meal,

the skim-milk formed half of the mixture. This meal was also retested to insure its alkalinity as it entered the stomach.

Calculation of Error.—It could not be expected that work of this kind would be trustworthy for comparisons, excepting in marked differences. To ascertain what our error would be in infants who had not been previously tubed or selected for investigation because of their particular adaptability, we made sixteen observations on infants taken at random. These are recorded in Table 1. In most of these cases the infants were allowed to go three and a half hours after a feeding before giving the test-water. If the stomach was empty we introduced 45 c.c. of plain water through the catheter, recovering it immediately by expression and syphonage. In each case the water was completely delivered to the stomach, none being allowed to remain in the tube. The syphonage was started by expression, one of us pressing over the epigastrium. It will be seen that our greatest error in recovering the contents is 5 c.c. and that the error is seldom greater than 3 c.c. In most instances a little mucus was recovered, As stated before, the infants with which this investigation had to do were carefully selected and caution was observed to wash and drain the stomach. In these babies our error[1] was less than 3 c.c.

TABLE 1.—SIXTEEN INVESTIGATIONS ON INFANTS TAKEN AT RANDOM TO DETERMINE ROUGHLY THE ERROR IN RECOVERING IMMEDIATELY BY MEANS OF STOMACH TUBE, A GIVEN AMOUNT OF FLUID DELIVERED TO THE STOMACH BY GAVAGE*

No.	Name	Interval Since Last Feeding hours	Condition of Stomach	Amount of water Given, c.c.	Amount of water Recovered, c.c.	Condition of water Recovered
1	Edwards	3½	Empty	45	40	About ½ c.c. mucus
2	Hessler	3½	Empty	45	45½	.....
3	Rush	3½	Empty	45	46	A little mucus
4	Kinyon	2½	Empty	45	46	Tinged yellow
5	Wilcox	3½	Empty	45	41	.....
6	Rush	3½	2 c.c.	45	43	Few fine curds
7	Mills	3½	Empty	45	40	A little mucus
8	Hessler	3½	Empty	45	45½	Plugs of mucus
9	Simmons	3½	Empty	45	46	Considerable mucus
10	Hackford	3½	Empty	45	49	2 or 3 c.c. mucus
11	Hacket	3½	Empty	45	44	½ c.c. thick mucus
12	Rush	3½	Empty	45	41	Few fine curds
13	Hatzke	3½	Empty	45	40	Little thick mucus
14	Mills	3½	Empty	45	44	Few fine curds
15	Nering	3½	Empty	45	45	A little mucus
16	Hessler	3½	Empty	45	41	A little mucus

* Greatest error in any one case 5 c.c. Average error 2.38 c.c.

SERIES I.—THE EFFECT OF ACID ON THE DUODENAL SIDE OF THE PYLORUS

The three sets of experiments recorded in Charts 1, 2 and 3 have to do with the duodenal side of the pyloric reflex. The control meals enter the stomach, remain there for a certain time, until the acid reflex on the stomach side causes the pylorus to open. The acid meal enters the

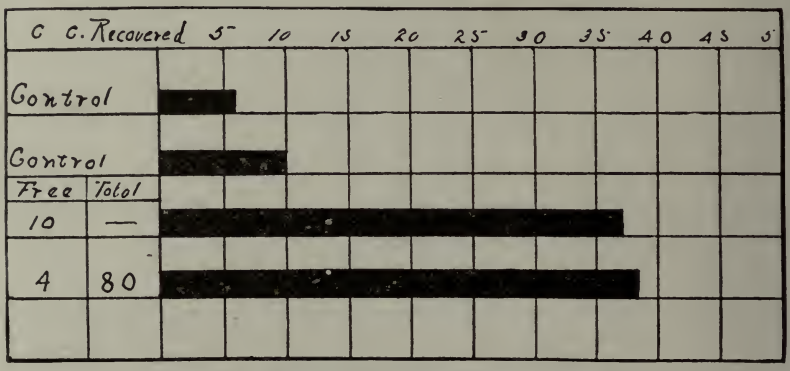


Chart 1.—Sustained duodenal reflex, Case 1.

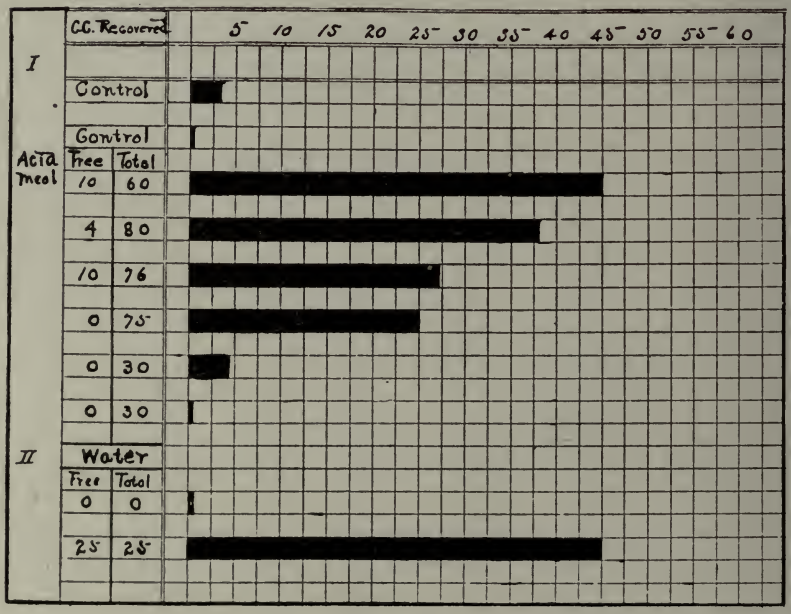


Chart 2.—Sustained duodenal reflex, Case 2. The secretion of this infant's stomach was always normal. There was no free HCl.

stomach with immediate stimulus for the pyloric opening reflex. As soon as it reaches the duodenum, in proportion to the amount ejected and its acidity, the pylorus remains closed. As our acid meal causes the pylorus to remain closed a comparatively long time, we speak of this as a sustained duodenal reflex, in contradistinction to the normal pyloric reflex and the delayed pyloric reflex recorded in our second series.

CASES 1 AND 2.—The data relating to these infants will be found in our previous report.[1] Both were in good health and gaining in weight. At no time in either case were we able to find any free hydrochloric acid. The delayed evacuation of the stomach is well shown in the acid meals. The higher the acidity, or the more acid present, the larger the amount recovered at the end of the period. This is particularly well shown in Case 2.

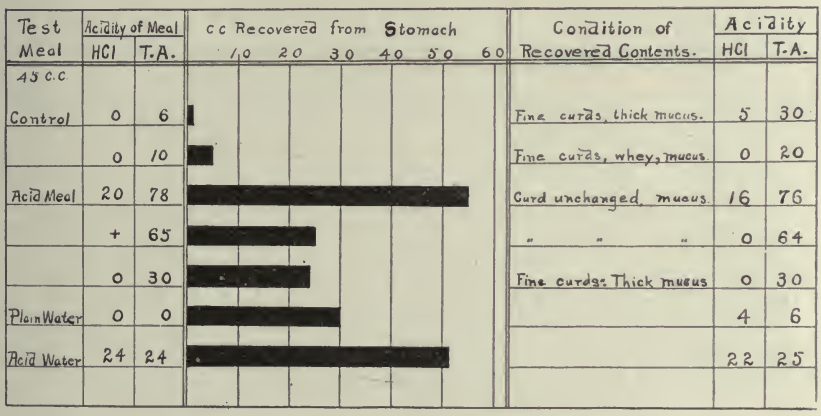


Chart 3.—Sustained duodenal reflex, Case 3. The secretion of this infant's stomach was always hypernormal. Free acid occurred in the fasting stomach.

CASE 3.—A well developed baby. History and physical examination negative. On referring to the series of stomach analyses (Table 2) it will be seen that the infant almost always secreted acid to the free point and at times gave a free acid value as high as 25 and 35, a true hyperchlorhydria for an infant. In addition to this, there were evidences of hypersecretion during the period of our observations. How long such a condition would continue without producing spasm, if it ever would, we cannot say, as the infant soon passed from under our observation.

There was nothing in Case 3 to suggest ulcer, either peptic or duodenal. We find in this case, three hours after an ordinary feeding, when the stomach is practically free from food remains, a free acid

value of 5. We also find that plain water leaves this baby's stomach much more slowly than does the control milk meal and the water meal in Case 2. It is believed, and supported by experiment, that water leaves the stomach almost directly. The reason for this, however, has never been satisfactorily explained. In this case we think the delayed evacuation of water can be explained by the presence of free acid in the fasting stomach and the hypersecretion. The water does not take up the acid but, as is known, may provoke a further secretion in this neurosis, hence the duodenal reflex is sustained longer than under normal conditions. In Case 2 we had no such condition to contend with. Free acid was never detected and the total acidity after an ordinary or test meal was never high, accordingly there was little or no neutralization to take place in the duodenum and the water passed on uninterruptedly into the gut.

TABLE 2.—RESULTS OF EXPERIMENTAL FEEDING IN CASE 3, SHOWING HYPERSECRETION AND HYPERCHLORHYDRIA*

Meal	Time in Stomach, Hours	Amount Fed, c.c.	Amount Recovered, c.c.	Free HCl	Total Acid
2-6-¾-W.	?	90	0	—	—
½ S. M. and water	¾	90	2	5	30
2-6-¾ W.	2	90	5	25	60
½ S.M. and water	¾	90	5	0	20
2-6-½-W.	2¾	90	4	35	70
2-6-½-W.	2½	90	7	35	70
Plain Water	¾	90	30	4	6
2-6-½-W.	?	90	2.5	15	60

*Abbreviations: 2-6-¾=2% fat, 6% sugar, ¾% protein. W=whey made up the balance of the mixture. ½ S.M.=Half skim milk and water.

DETAILED ACCOUNT OF EXPERIMENTS

Control Meal No. 1. Infant 36 Days Old. May 11, 1910

8:50 a. m. Three hours and fifty minutes after 90 c.c. 2-6-¾-whey mixture; nothing obtained through tube; stomach washed with 90 c.c. water; all recovered, containing about 1 per cent. fine curds and mucus.

8:55 a. m. Fed 90 c.c. half skim-milk and water, through a No. 14 catheter; total acidity of food; fat .9 per cent.

9:40 a. m. (45 minutes) 2 c.c. whey; mucus thick; a few very fine curds recovered; stomach washed with 85 c.c. water; 83 c.c. containing about 2 per cent. thick mucus and a few small curds recovered. Free HCl 5; total acid 30.

Control Meal No. 2. Infant 37 Days Old. May 12, 1910

8:40 a. m. Two hours and forty minutes after 90 c.c. of 2-6-¾ whey mixture; 5 c.c. recovered, containing 50 per cent. curds, and mucus thick. HCl 25; total acid 60. Stomach washed with 40 c.c. warm water; 40 c.c. recovered practically clear.

8:45 a. m. Five minutes later, fed by gavage 90 c.c. half skim-milk and water; total acid 10; fat .8 per cent.
9:30 a. m. (45 minutes) 5 c.c. recovered; whey containing a few small curds and mucus. HCl 0; total acid 20.

Acid Meal No. 1. Infant 38 Days Old. May 13, 1910

6:00 a. m. 90 c.c. 2-6-½ whey nursed.
8:45 a. m. 4 c.c. recovered, containing 25 per cent. thick mucus and a few small curds, HCl 35; total acid 70. Stomach washed with 45 c.c. warm water; all recovered, containing 2 per cent. thick mucus.
9:00 a. m. Fed 90 c.c., half skim-milk and water acidified by gavage. Free HCl 20; total acid 78.
9:45 a. m. (45 minutes) 55 c.c. milky material recovered containing 20 per cent. very fine curds and thick mucus. The whey is very milky. HCl 16; total acid 76. Stomach washed with 45 c.c. warm water; all recovered; slightly opaque with milky material.

Acid Meal No. 2. Infant 42 Days Old. May 16, 1910

9:45 a. m. 90 c.c. half skim-milk and water, acidified, fed. Free HCl trace; total acid 65.
10:30 a. m. (45 minutes) 25 c.c. recovered. Same condition as when it entered stomach, excepting a little mucus. HCl 0; total acid 64. Stomach washed with 80 c.c. water; 82 c.c. recovered; slightly turbid.

Acid Water Meal Experiment. Infant 42 Days Old. May 16, 1910

6:00 a. m. 90 c.c. 2-6-½ whey nursed.
8:30 a. m. 7 c.c. recovered containing 50 per cent. thick mucus and curds. HCl 35; total acid 70. Stomach washed with 45 c.c. warm water; 46 c.c. recovered, slightly cloudy.
8:40 a. m. Fed 90 c.c. plain water by gavage.
9:10 a. m. 30 c.c. recovered containing a little thick mucus. HCl 4; total acid 6.
9:13 a. m. Fed 90 c.c. acidified water, HCl 24, by gavage.
9:43 a. m. (30 minutes) 51 c.c. recovered. Free HCl 22; total acid 25.

Acid Milk Meal No. 3. Infant 43 Days Old. May 17, 1910

8:55 a. m. 2.5 c.c. containing 60 per cent. thick mucus and curds recovered from stomach. Free HCl 15; total acid 60. Stomach washed with 95 c.c. warm water; 90 c.c. recovered containing 2 per cent. fine curds and mucus.
9:00 a. m. 90 c.c. half skim-milk and water, total acidity 30, given by gavage.
9:45 a. m. (45 minutes) 24 c.c. clear whey containing a few small curds and considerable thick mucus recovered. HCl 0; total acid 30. Stomach washed with 45 c.c. warm water; all recovered practically clear.

SERIES II.—THE EFFECT OF ACID ON THE STOMACH SIDE OF THE PYLORUS

In this series the control meal enters the stomach under the same conditions as before; there is a food stimulus for the secretion of acid to open the pylorus, while in the basic or alkaline meal, although the food

stimulus, so far as we know, is exerted on the secretory mechanism of the stomach, the presence of alkali to the point of saturation of the protein delays the acid in reaching the point for stimulation of the opening reflex; hence at the end of forty-five minutes a very much larger amount is recovered than in the control experiments—not 5 or 10 c.c., but double and treble the amount.

It will be observed in these experiments that at times we recovered as much as 15 c.c. more, at the end of the period, than we had put in. This was at a time preceding the opening reflex and represents roughly the amount of gastric juice secreted. In Case 4 we recovered at the end of thirty minutes 15 c.c. more than we put in; at the end of forty-five minutes we recovered a few c.c. more than we originally put in, but about 12 c.c. less than we reintroduced into the stomach. In this experiment, if we had again introduced the contents removed at forty-five minutes, ten minutes later we might have experienced what we have on more than one occasion—the stomach almost empty. The pyloric reflex has just begun to operate and because of the low acidity of the food either a large gush or a series of rapid short gushes has evacuated the stomach. On one occasion at forty-five minutes nearly all the food was present in the stomach, and no curd formation had taken place; in fifty minutes only a small amount of curded material could be recovered.

These experiments, we think, give abundant proof that the pylorus is governed by acid on both sides of the pyloric ring and confirm, in man, the experiments in animals done by Pawlow, Cannon and others.

CASE 4 (Charts 4 and 5).—Baby G., an apparently normal infant. History and physical examination negative. On referring to the series of stomach analyses, Table 3, it will be seen that this infant never secreted free acid and that the total acid was never excessively high.

TABLE 3.—RESULTS IN FREE HCl AND TOTAL ACIDITY IN FEEDING EXPERIMENTS IN CASE 4

Meal	Time in Stomach, Hours	Amount Fed, c.c.	Amount Recovered c.c.	Free HCl	Total Acidity .....
2-6-½	1¾	75	27	0	32
½ S.M. and Water	¾	45	13?	0	26
2-6-½ W.	2¾	45	26	0	32
½ S.M. and Water	5/6	45	?	0	15
2-6-½ W.	½	30	30	0	44
2-6-½ W.	2¾	90	1	0	—
½ S.M. and Water	⅔	45	?	0	12
2-6-½ W	...	..	..	.	..

DETAILED ACCOUNT OF EXPERIMENTS IN CASE 4

Control Meal No. 1. Infant 30 Days Old. May 25, 1910

7:30 a. m. Nursed 75 c.c. 2-6 ½ mixture.

9:13 a. m. 27 c.c. recovered, containing 15 per cent. curds and thick mucus. HCl 0; total acid 32. Stomach washed with 90 c.c. water; 90 c.c. recovered, containing 2 per cent. curds.

9:20 a. m. 45 c.c. half skim-milk and water, total acidity 10, given by gavage.

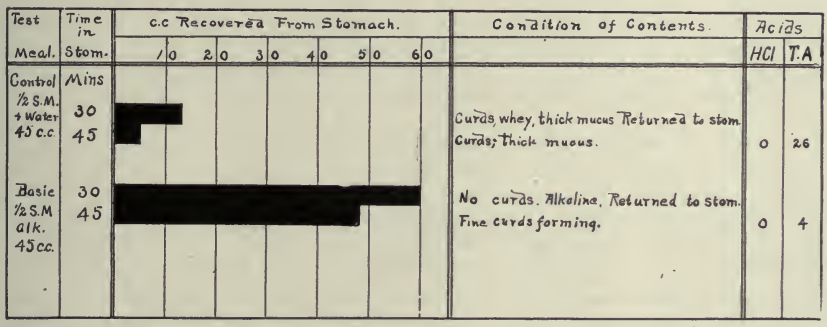


Chart 4.—Delayed pyloric reflex. Case 4, Experiment 1, showing the effect of alkali on stomach evacuation. The secretion of this infant's stomach was always normal.

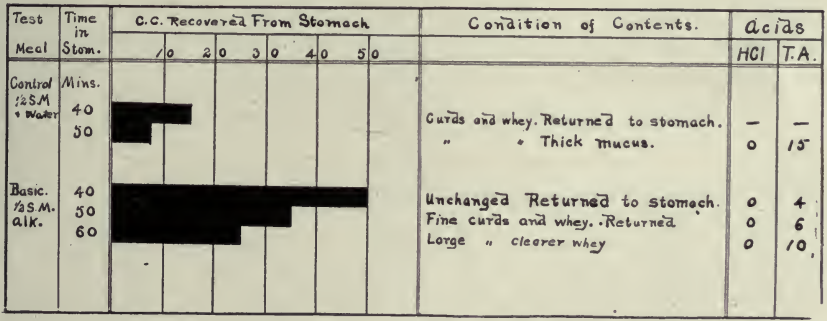


Chart 5.—Delayed pyloric reflex. Case 4, Experiment 2, showing the effect of alkaline contents on stomach evacuation.

9:50 a. m. (30 minutes) 13 c.c. of fluid were expressed, consisting of whey, medium sized curds, and thick mucus. This was returned to the stomach.

10:05 a. m. (45 minutes) 15 c.c. of fluid were expressed consisting of 20 per cent. large curds and some thick mucus. HCl 0; total acid 26. Stomach washed with 90 c.c. water; 88 c.c. returned practically clear.

Basic Meal No. 1. Infant 30 Days Old. May 25, 1910

10:10 a. m. 45 c.c. of half skim-milk and water, rendered basic with lime water, were given by gavage.

10:40 a. m. (30 minutes) 60 c.c. recovered; no curds; reaction alkaline to litmus; returned to stomach.

10:55 a. m. (45 minutes) 49 c.c. Fine curds beginning to form. HCl 0; total acid 4. Stomach washed; only a few fine curds returned.

Remark: It will be observed that thirty minutes after feeding we recovered 15 c.c. more than was introduced, and that no curd formation was present; that fifteen minutes later curds had formed and 45 c.c. were recovered. No stimulus to pyloric opening was present until about this time. The 15 c.c. doubtless represents grossly the amount of gastric juice secreted during the first thirty minutes' stay in the stomach. See Chart 4.

Control Meal No. 2. Infant 32 Days Old. May 27, 1910

6:00 a. m. Fed 45 c.c. 2-6-½ whey mixture.

8:40 a. m. 26 c.c. recovered; 30 per cent. curds and thick mucus. HCl 0; total acid 32. Stomach washed with 90 c.c. warm water; all recovered, containing a little over 1 per cent. fine curds and mucus.

8:45 a. m. 45 c.c. half skim-milk and water, total acid 9, given by gavage.

9:25 a. m. (40 minutes) 15 c.c. expressed, consisting of fine curds and whey. Returned to stomach.

9:35 a. m. (50 minutes) 8 c.c. fluid containing 20 per cent. medium small curds and a little thick mucus recovered. HCl 0; total acid 15. Stomach washed with 90 c.c. water; 89 c.c. recovered, containing a few fine curds and mucus hardly measurable by centrifuge.

Basic Meal No. 2. Infant 32 Days Old. May 27, 1910

9:40 a. m. 45 c.c. one-half skim-milk and water, rendered basic with lime water, were given by gavage.

10:20 a. m. (40 minutes later) 50 c.c. recovered; no distinct curds; appears about the same as when introduced. Total acid 4; returned to stomach.

10:30 a. m. (50 minutes) 35 c.c. recovered; distinct fine curds and whey. Free acid 0; total acid 6. Returned to stomach.

10:40 a. m. (60 minutes) 25 c.c. recovered; curds larger and more separated from the whey. HCl 0; total acid 10. Stomach washed clear.

Basic Meal No. 3. Infant 36 Days Old. May 31, 1910

5:00 a. m. 75 c.c. 2-6-½ whey mixture.

8:00 a. m. 15 c.c. 2-6-½ whey mixture.

8:30 a. m. 30 c.c. of whey containing 2 per cent. curds and a little thick mucus recovered. HCl 0; total acid 44. Stomach washed with 130 c.c. warm water. All recovered plus a little mucus.

8:55 a. m. 45 c.c. one-half skim-milk and water, rendered basic, given by gavage.

9:35 a. m. (40 minutes) 35 c.c. recovered, containing 20 per cent. curds, whey and thick mucus. Tube was repeatedly blocked by the curds. HCl 0; total acid 8. Stomach washed with 90 c.c. warm water; 90 c.c. recovered, containing a few small curds and considerable thick mucus.

Control Meal No. 3. Infant 38 Days Old. June 2, 1910

6:00 a. m.	90 c.c. 2-6-½ whey mixture.
8:45 a. m.	1 c.c. thick mucus recovered. HCl 0. Stomach washed with 45 c.c. warm water; all recovered, perfectly clear excepting a little mucus.
8:55 a. m.	45 c.c. plain one-half skim-milk and water were given by gavage; total acidity 8.
9:15 a. m.	(20 minutes) 45 c.c. recovered; fine curds beginning to form. Returned to stomach.
9:25 a. m.	(40 minutes) 30 c.c. recovered; curds more distinct; mucus more marked. Returned to stomach.
9:35 a. m.	(50 minutes) 15 c.c. recovered, whey containing 5 per cent. large curds; tube blocked with thick mucus. HCl 0; total acid 12. Stomach washed clean.

It may be asked what practical bearing these observations have on gastro-enterologic therapy and on our knowledge of gastro-enteric diseases. It was Dr. Cowie's object in starting these observations to see if the management of pyloric stenosis in infants, both true and false, could be put on a scientific basis. Most cases of this character have been treated without reference to the pyloric reflex or the altered physiologic conditions present. We believe there is a certain group of cases in which these are important factors to determine. It would seem at least possible to recognize varying degrees of stenosis and readily to differentiate them from what may be called pseudo-stenosis or spasm and to enable us to observe the effect of the reaction of the food given on the duration of the duodenal closing reflex, which seems to be an important factor in many cases. This will be considered in a later article.

CONCLUSIONS

1. The pyloric opening and closing reflex can be easily demonstrated in infants' stomachs.

2. In experimental acid stomach contents the duodenal closing reflex is sustained and consequently the evacuation of the stomach is delayed.

3. In experimental alkaline stomach contents the pyloric opening reflex is delayed and consequently the evacuation of the stomach is delayed.

4. Free acid is not necessary for pyloric opening. Its presence has a tendency to provoke prolonged duodenal closing in an infant.

5. In hypersecretion in infants protein-containing food appears to leave the stomach more readily than water because of its binding property for acid.

Lawrence Building.

PYLORIC STENOSIS IN OLDER CHILDREN, WITH REPORT OF A CASE OF PYLORIC SPASM ENDING FATALLY

EDWIN E. GRAHAM, A.B., M.D.
Professor of Diseases of Children, Jefferson Medical College
PHILADELPHIA

It is not my intention to study in this paper the condition spoken of as congenital pyloric stenosis in infants, but to consider stenosis of the pylorus in children who have passed the period of infancy. The study of the condition in older children must, however, embrace those patients in whom the condition has persisted from infancy into later childhood, as well as those cases in which infancy has been free from all symptoms of pyloric stenosis, but in which the symptoms appeared months or years later.

At the outset of this study one is immediately impressed by the fact that while medical literature is crowded with articles on congenital hypertrophic pyloric stenosis and pyloric spasm in infants, there has been, as far as I am aware, little written exclusively on the condition in older children.

The discussion in all of these papers deals with the problem as to whether the condition is congenital or not; as to the cause of the hypertrophy of the circular muscular fibers at the pylorus; as to whether in a given case the condition is one of pyloric spasm simply, or hypertrophic stenosis simply, or both spasm and hypertrophy, and as to the necessity for an operation.

The etiology of these congenital or early cases of pyloric stenosis has been considered as due, perhaps, to gastric hyperacidity, or at least to some disturbance of gastric secretion and consequent gastric indigestion. Other causes are hyperplasia at the pylorus, edema of the mucous membrane of the pylorus and pyloric spasm. The causes of spasm are not clear. It may be due to a toxemia, to gastric dilatation, to a change in the gastric secretion, or it may be nervous in origin. The classical symptoms are vomiting, constipation, progressive loss in weight, scanty urine, visible peristaltic waves, and possibly finding a tumor at the pylorus.

The treatment ordinarily advised is, feeding, stomach-washing, opium, poultices to epigastrium, saline enemata for the purpose of absorption of liquid, nutrient enemata, operation.

A study of the subject of organic pyloric stenosis as found in American, English, German and French literature has impressed forcibly on me the belief that a careful clinical examination of children and young adults will result in bringing to light a fair proportion of cases of organic stenosis during this period of life. The condition was long overlooked in infants; and while not flattering to clinicians, it is, I believe, nevertheless true that the condition is now being overlooked in the older child and young adult.

Children and young adults[1] who present gastric symptoms that continue for months or years, and especially if vomiting and epigastric pain are present, may be suffering from organic pyloric stenosis, and if such patients have been treated for a long time medicinally without benefit, the probability of there being organic pyloric stenosis increases. Many such cases have finally come to operation, and a pyloric stenosis found by the surgeon at operation.

The reason why medical treatment failed in these patients is then clear. Permanent changes have taken place in the gastric secretory apparatus, the result of the long continuance of the hypertrophic stenosis, and a cure by medical treatment is impossible. An early recognition of the pyloric obstruction should in a fair, or probably in a large, proportion of these cases lead to their cure by medical rather than surgical treatment. This seems at least probable, if one is to reason by the results obtained in pyloric stenosis in infants and older children. A study of the cases in infants and older children treated medically, shows conclusively that the majority of those infants who suffer from a mild degree of hypertrophic pyloric stenosis are cured by the physician and do not come to operation. Heubner[2] reports nineteen cured in twenty-one infants; Bendix[3] thirty in thirty-two cases; Hutchison[4] thirteen in fourteen cases; Stark[5] eleven out of twelve cases; Bloch[6] six patients, all recovered.

I do not wish to be understood as implying that there are not patients who require operation. I believe that the position taken on the question

1. Maylard: Brit. Med. Jour., July 11, 1908, p. 71.
2. Heubner: Therap. d. Gegenw., 1906, viii.
3. Bendix: Med. Klin., 1909, vi, 1813.
4. Hutchison, Robert: Clin. Jour., Sept. 9, 1908.
5. Stark: Zentralbl. f. Kinderh., 1909, xiv, 5.
6. Bloch: Jahrb, f. Kinderh., 1907, lxv, 317.

of operation by Robert Hutchison,[4] "that operation is never in any circumstances justified in these cases," is an extreme one, but that most of the cases of slight and moderate pyloric stenosis can be cured by medical treatment is my firm belief.

It is an accepted fact that many patients live into advanced adult life, who at autopsy show congenital pyloric stenosis. Rudolph Mayer[7] reports thirty-one such cases. Cautley and Dent[8] report three cases of pyloric stenosis at the ages of 6, 11 and 22 years, respectively, and believe they were probably congenital. Mayo Robson reports one case, Lauderer[9] ten and William Russell[10] three cases.

There is probably no doubt that congenital pyloric stenosis of a mild grade may remain latent for months and probably for years, and cases of organic pyloric stenosis have been observed during the second and third years of life, where a distinct insufficiency of motility, together with hyperacidity, existed. There is probably hardly any year between early infancy and well advanced old age that does not show cases of pyloric stenosis in which the patients have come to operation. Some of these patients have had gastric symptoms from childhood; in others the symptoms vary from a few months to a number of years. Rosenheim[12] reports a case in a child who had always enjoyed good health until an attack of measles at the age of 5 years, from which he made a good recovery. Three months later the child began to vomit and continued to vomit almost every day. When 6½ years of age he was operated on and found to be suffering from hypertrophic pyloric stenosis. The case ended in recovery. Osler reports a case of hypertrophic pyloric stenosis in a child that lived until the third year.

There is much room for thought in the study of the cases in which the hypertrophic stenosis is not sufficient in amount to produce dangerous symptoms in infancy. The hypertrophy gradually increases in amount, the stenosis becomes more marked, and in later years the child presents the symptoms directly and indirectly produced by the stenosed pylorus. Beardsley reports a case at the age of 4 years, Sonnenberg one at 5 years, and Hansy one at 11 years (Cautley[13]).

7. Mayer, Rudolph: Virchow's Arch. f. Path. Anat., 1885, cii, 413.
8. Cautley and Dent: Tr. Roy. Med. and Chir. Soc., 1902, lxxxvi.
9. Lauderer: Tübingen, 1879.
10. Russell, William: Brit. Med. Jour., July 11, 1908.
11. Bernheim (Zurich): Deutch. med. Wchnschr., 1908, p. 1830.
12. Rosenheim: Berl. klin. Wchnschr., 1899, xxxii, 703.
13. Cautley: Diseases of Children, 1910, p. 264.

Then there are cases that present exactly the opposite picture. The symptoms of hypertrophic pyloric stenosis are very severe in infancy; the babies are so ill that it seems as if they must surely die. They recover, however, and at the age of 3 or 4 years are apparently perfectly well. Robert Hutchison has reported such cases.

The question naturally arises, what has occurred in these cases? Has the congenital hypertrophy of the pylorus largely or partly disappeared? Has the compensatory hypertrophy of the stomach muscles been sufficient to overcome the original condition, and has no gastric dilatation occurred, or has it been a combination of both conditions? Cases are reported in which apparently no gastric dilatation has occurred, and the evidence in such cases points strongly to absorption of the hypertrophy.

What is the explanation of the very large percentage of recoveries reported by certain observers — Heubner, Bendix, Hutchison, Stark, and Bloch? I believe it is as follows: Many of these cases are instances of pyloric spasm; others are cases of slight hypertrophic pyloric stenosis; in still others, both spasm and a mild degree of hypertrophy exist, and if one is ready to admit that a slight amount of hypertrophic pyloric stenosis may be largely or in part absorbed, the explanation is quite satisfactory. Stiles, who has operated on many of these patients, claims that true congenital hypertrophic stenosis of the pylorus is rare, and when it does occur, should be treated surgically. Cautley is of about the same opinion, but believes that very mild cases of this disease may recover under medical treatment. Cases of this character may, and probably do, in some instances, show gastric symptoms and evidence of plyoric stenosis in later life, since persistent stenosis in the older child is represented by, first, a period of compensatory stomachic muscular hypertrophy; this is followed by a period which may exist from the inception of the stenosis which represents stagnation and the slow emptying of the stomachic contents; and lastly, retention, or the failure of the stomach ever to completely empty itself. Is it not possible to recognize these cases clinically? Should they come to operation undiagnosed?

The following conclusions in regard to hypertrophic pyloric stenosis in older children and young adults seem to me to be justifiable:

1. Pyloric stenosis is present in children and young adults more commonly than is supposed.

2. The age at which it manifests itself depends on the degree of stenosis present.

3. Pyloric stenosis may be latent for years.

4. It is found by the surgeon during childhood and young adult life, and its early recognition by the physician is important from the standpoint of early medical or, if necessary, surgical treatment.

5. The entire disappearance of all the classical symptoms of congenital hypertrophic stenosis, and the apparent health of the infant during its subsequent early childhood, suggest the probability of an absorption of the hypertrophy, especially as no gastric dilatation may develop later in life.

CASE REPORT

It may be interesting in this connection to give the history of a case of pyloric spasm in a boy aged 6½ years, whose general health during infancy and childhood had been first-class until a few months before his death; who presented during the last few months of his life a typical picture of pyloric spasm; who came to autopsy, and in whom no disease of the pylorus or stomach was found post mortem.

History.—W. L., aged 6½, was admitted to the Jefferson Hospital March 8, 1911, under the care of Dr. Nassau, and I was asked by Dr. Nassau to see him a few days after his admission. The history of the case was as follows: Mother, father, two sisters, and two brothers were in good health; no hereditary history. The child had pertussis one year previously. The left eye was injured by a fall in July, 1909, and the eye was enucleated in November, 1910; he gained 9 pounds in three weeks after the operation. Six weeks previous to admisison to Jefferson Hospital he began to vomit. Vomiting occurred at irregular periods, bore no relation to the taking of food, and was most frequent in the morning. Vomiting was preceded by nausea and restlessness, which was relieved by vomiting. Vomiting might be absent for several days. He had no pain, no blood in the vomitus; had been rapidly losing weight, and was becoming much weaker, and had been confined to bed for one week. There was no history of chills or fever.

Examination.—The patient was poorly nourished; pupil of right eye was large, but reacted well to light and accommodation; a few submaxillary glands were palpable on both sides; tongue coated, with clean, pink margins. Chest poorly developed; ribs prominent; lungs normal. Abdomen was scaphoid; walls thin; no areas of tenderness or rigidity; no pyloric tumor could be felt. Urine, acid, 1,010, no albumin, no sugar, no acetone or diacetic acid; urea 2.9 per cent.; few leukocytes; no blood, no casts. March 17, 1911, the child had vomited three times in the previous two days; no vomiting had occurred during the two days previous to that; there was constipation; weight with night clothes and sandals, 35¾ pounds. The mother stated that he weighed 57 pounds two and one-half months previously. Report on the vomitus showed no hyperacidity and that bile was present. March 20 a bismuth meal was given. An *x*-ray plate seven hours after the meal showed the bismuth distributed in the stomach, but no trace of bismuth in the duodenum. This plate proved conclusively that food failed to pass normally from the child's stomach in the usual period, as a normal stomach will clear itself of a bismuth meal in from five to seven hours. Another plate showed the gold ball which had been placed in the orbit after enucleation of the eye. I did not learn until afterward that the eye was removed for sarcoma.

The stools were small, yellow and well digested. The amount usually vomited at one time was never much more than the amount taken at one feeding. The Morro test was negative.

March 21. The child vomited first Jan. 20, 1910. The vomiting gradually got worse; formerly there was less effort in vomiting, but now vomiting was more violent and retching. He had been constipated all his life. The patient took and retained 14 ounces of water; no tumor was palpable with the stomach so distended. Examination of the unoperated eye showed no lesion of the fundus. The pulse was 130 to 150; temperature 97 F. to 102 F. The treatment consisted of liquid nourishment, nutrient enemata, stimulants, bromid or soda and alkalies. As the patient was not improving under medical treatment, and there was evidently from the *x*-ray plates a growth developing in the eye that had been previously operated on, and especially in view of the fact that I had learned that the eye had been operated on for sarcoma, a second operation on the eye was performed by Dr. Howard Hansell March 25, 1911.

Operation on the Eye.—The orbital cavity was completely filled with a dense hard growth, irregular in outline and extending forward to the commissure. The overlying conjunctiva appeared to be healthy. In operating for the removal of the growth, a horizontal incision was made through the conjunctiva from one canthus to the other. Through this opening the finger was introduced and by manipulation the tumor was enucleated and removed in sections. The largest portion included in its center the shrunken sclera, which partly enclosed a gold ball which had been inserted at the time of the enucleation of the globe some months previously.

The floor of the orbit was extensively necrosed and communicated by a large rough-edged, round opening with the antrum of the same side. The floor and outer wall of the orbit were denuded of periosteum, and contained several necrotic areas. The sphenoidal fissure was much larger than normal, by reason of adjacent diseased bone.

The patient rallied fairly well from the operation, but continued to grow weaker; vomiting continued; the amount of nourishment taken was very small, and he died April 6.

Necropsy.—Post-mortem record of W. L. Date of post-mortem, April 7, 1911, 12 noon.

Pathologic Diagnosis.—Sarcoma of liver, enlarged mesenteric lymph-nodes.

External Examination.—Body is that of an extremely emaciated male child. The left orbit contains a small quantity of gauze, which is saturated with purulent material. Rigor mortis present but easily broken up. Post-mortem suggillation is marked posteriorly.

Internal Examination.—Musculature wasted and subcutaneous fat very scant.

Peritoneum: Smooth and glistening; cavity contains a small amount of clear, straw-colored fluid; liver extends to costal margin, mid-clavicular line. The intestine is partially collapsed; this condition to be described later.

Left Pleura: Free from adhesions; surfaces are smooth and glistening; cavity contains a small amount of straw-colored fluid.

Right Pleura: Resembles its fellow of opposite side.

Pericardium: Smooth and glistening; cavity contains small amount of clear serum.

Heart: Normal in size. Right auricle—endocardium smooth and glistening; cavity filled with semifluid blood.

Left Lung: Crepitates throughout; cut surface pinkish-red in color, and shows no gross lesions; weight, 160 gm.

Right Lung: Same. Weight, 150 gm.

Spleen: Measures 6x3x2 cm., is soft and of purplish-red color; weight, 160 gm.

Left Kidney: Measures 6x3.5x2.5 cm., red in color; cuts with normal resistance; cortex bears normal relationship to pyramids and is red and injected; capsule strips readily, revealing a smooth surface; weight, 75 gm.

Right Kidney: Resembles its fellow; weight, 70 gm.

Ureters and Bladder: Show no gross lesions.

Stomach: Contains a small amount of yellowish material; capacity of 175 c.c. The mucous membrane shows some slight post-mortem discoloration. The pyloric orifice is patulous, and the pyloric ring seems to be normal in thickness.

Duodeum: Mucosa bile-tinged, but shows no macroscopic lesions.

Liver: Normal in size, reddish color, capsule smooth, cuts with normal resistance. In the right lobe near the anterior margin there is a firm, yellowish nodule measuring 4 cm. in diameter, sharply demarcated from the surrounding liver tissue. Remainder of organ apparently normal.

Pancreas: Normal in size and color, and shows no noteworthy lesions.

Intestines: Mesenteric lymph-nodes are enlarged, firm and of reddish color. The small intestine at a distance of 20 cm. from the ileocecal junction is collapsed for a distance of about 50 cm. Remainder of organ shows no lesions.

Vena Cava and Aorta: Normal.

Microscopic Diagnosis.—Tumor of Liver: Small round-celled sarcoma.

Pylorus: Normal.

Mesenteric Glands: Hyperplasia of lymphoid tissue.

Brain: Showed nothing.

The case of pyloric spasm here reported and coming to autopsy is to me of great interest. It was unconnected with any organic disease of the stomach, or with any change in the normal gastric secretion. Spasm of the pylorus in older children is spoken of by many authors, and is usually described as being associated with severe pain, perhaps little or no vomiting, and often connected with disease of the pancreas, appendix or gall-bladder, gastric ulcer, or distinct change in the gastric secretions. Pain was absent in my case; vomiting was the one prominent symptom, and loss in weight was rapid and extreme. In these two particulars, absence of pain and violent and persistent vomiting, it differs from the cases described by most writers. After the enucleation of the eye, the vomiting lessened, and in three weeks the boy gained 9 pounds. The vomiting ceased for five or six weeks after the first operation, and then gradually increased in frequency and severity until the second operation, when the sarcomatous mass was thoroughly removed from the orbit.

The case appears to belong to the group of so-called nervous vomiting, of reflex origin, associated primarily with disease of the eye, and later, aggravated by metastasis in the liver. Reflex vomiting of eye origin is independent of the taking of food, and while it lasts is persistent. The

vomiting of eye origin does not last for days, and is usually followed by an ability to take and retain food. The primary operation was followed by entire cessation of vomiting, and a gain in weight. The sarcoma returned in the orbit, metastasis occurred in the liver and both these conditions caused, in my opinion, a severe return of this gastroneurosis. The operation of cleaning out the orbit only slightly affected the vomiting; the boy was in a deplorably weak condition at the time of the operation, and the sarcoma of the liver was probably instrumental in causing a continuance of the vomiting, which persisted, although in a less degree, until his death. In my opinion, the second operation neither hastened nor retarded death.

The stomach through the sympathetic and cerebrospinal nerves is connected with practically all organs and tissues in the human body, and it has been demonstrated that pyloric spasm can be produced artificially by stimulation of the vagus. The contraction of involuntary muscular tissue, the source of the contraction being outside the stomach, is at least probable.

Is pyloric spasm unassociated with pain and with persistent vomiting, a common condition, or even an occasional condition in older children? It certainly clinically does not resemble the cases described as associated with gastric ulcer,[14] and gall-stone colic in which the pain is excessive and vomiting not a marked symptom. Periodic pyloric spasm may occur at the menstrual period,[15] unassociated with any disease of the stomach, or with spasm in any other portion of the body, and under such conditions is probably a primary spasm of the pylorus, a motor neurosis. Lauder Brunton's observations tend to show that pyloric spasm may accompany migraine, and be a manifestation of a neurosis.

A number of cases of infantile pyloric spasm have been followed up to the age of 5 years and older, and found to be in first-class health, and a neurotic family history is not found in quite a considerable number of such cases. The clinician should not lose interest in these babies after they pass beyond the period of infancy, and an effort should be made to follow their subsequent histories, especially with reference to any gastric symptoms.

Cases of infantile pyloric spasm have been kept under observation for years.[17] All the symptoms may persist until the third year, and the

14. Fairchilds: Iowa Med. Jour., Des Moines, 1910-11, xvii, 212.
15. Hemmeter: Diseases of the Stomach, Ed. 3, p. 144.
17. Heubner: Berlin, Therap. d. Gegenw., 1906, viii, 433.

child may remain nervous and anemic for years afterward. In other cases, solid food cannot be given until the child is 3 or even 5 years old. In still other cases of spasm, vomiting may persist until the child is 4 years old or older, and the peristaltic waves may continue until the child is over 4 years of age.

Cases diagnosed as cyclic vomiting have come to autopsy[18] and the lumen of the pylorus has been found to be very small, with a distinct hypertrophy. In these cases the children may be 4 or 5 years of age, the symptoms of epigastric pain and vomiting having been present since birth, returning at irregular intervals of months, and the children being apparently perfectly well between the attacks.

I do not mean to give the impression that cyclic vomiting and pyloric spasm are not two entirely different conditions, but to suggest the advisability of considering the possibility of pyloric spasm producing symptoms that resemble closely those of cyclic vomiting.

What are the causes of the pylorospasm in infancy that disappears in later childhood? Half of these children are breast-fed, and it seems to me unnatural to claim, as does von Starck, that the unaccustomed presence of food in the stomach produces an irritation of the gastric mucosa and so causes the spasm.

A clearer understanding of the etiology in infants may help us in the recognition and study of the condition in older children.

---

18. Russell: Proc. Roy. Soc. Med., London, 1909-10, iii, Sect. Dis. Child., 78.

MUSCULAR HYPERTROPHY OF THE PYLORUS IN INFANCY

HENRY LARNED KEITH SHAW, M.D., AND THOMAS ORDWAY, M.D.
ALBANY, N. Y.

This may be defined as an affection occurring in young infants characterized by forcible vomiting, constipation, visible peristalsis and frequently a palpable tumor at the situation of the pylorus produced by a marked increase in its muscle fibers. The disease has been described under the names "Hypertrophic Pyloric Stenosis in Infants," "Congenital Spastic Stenosis," "Congenital Pyloric Stenosis," and "Spastic Hypertrophic Pyloric Contracture."

Osler discovered a typical description of this disease written by Dr. Hezekiah Beardsley in a volume entitled "Cases and Observations by the Medical Society of New Haven County in the State of Connecticut," published in New Haven in 1787. It will not be out of place to quote liberally from this paper which is remarkable for the accuracy of observation and quaintness of diction.

"A child of Mr. Joel Grannis, a respectful farmer in the town of Southington, in the first week of its infancy, was attacked with a puking, or ejection of the milk, and of every other substance it received into its stomach almost instantaneously, and very little changed. The feces were in small quantity and of an ash color, which continued with little variation till its death. For these complaints a physician was consulted, who treated it as a common case arising from acidity in the prima via; the testaceous powders and other absorbents and correctors of acid acrimony were used for a long time without any apparent benefit. * * * I was at first inclined to attribute the disorder to a deficiency of bile and gastric juices, so necessary to digestion and chylification, joined with a morbid relaxation of the stomach, the action of which seemed wholly owing to the weight and pressure of its contents, as aliment taken in small quantities would often remain on it, till, by the addition of fresh quantities, the whole, or nearly all, was ejected; but his thirst, or some other cause, most commonly occasioned his swallowing such large draughts as to cause an immediate ejection, and often-times before the cup was taken from his mouth. * * * A number of the most respectable medical characters were consulted and a variety of medicines were used to little or no effect. His death, though long expected, was sudden, which I did not learn till the second day after it took place. This late period, the almost intolerable stench, and the impatience of the people who had collected for the funeral prevented so thorough an examination of the body, as might otherwise have been made. * * * I next examined the stomach, which was unusually large, the coats were about the thickness of a hog's bladder when fresh and distended with air; it contained about a wine pint of fluid exactly

Figs. 1, 2 and 3.—Visible peristalsis of the stomach, Case 3.

resembling that found in the vesicles before mentioned, and which I supposed to have been received just before his death. The pylorus was invested with a hard compact substance, or schirrosity, which so completely obstructed the passage into the duodenum, as to admit with the greatest difficulty the finest fluid; whether this was the original disorder, or only a consequence, may perhaps be a question. In justice to myself I ought to mention that I had pronounced a schirrosity in that part before the child's death."

Fig. 4.—Case 4. Stomach, duodenum, fragment of liver and gall-bladder; the upper part of the small intestine is sutured to the stomach just below the pylorus (natural size).

Williamson published an account of this condition in a 5-weeks-old infant with the autopsy findings in the London and Edinburgh *Journal of Medicine* in 1841.

No further mention of this disease in infants appeared in the literature until Hirschsprung, a Danish physician, reported two cases before the German Pediatric Society in 1887. He found that the pylorus was thickened and that the muscle fibers were increased. Pfaundler called attention to the fact that two distinct groups of cases had been classified under one head. He showed that there was both a functional and organic

Fig. 5.—Case 4. Same as Fig. 4. A portion of the anterior walls of the stomach, duodenum and jejunum have been removed showing the stenosed pylorus with greatly thickened walls (x-y). Here, as indicated, fragments have been removed for sectioning longitudinally (Figs. 6, 7, and 8) and transversely (Figs. 9 and 10). The natural and artificial food channels are indicated by arrows. z, large, patent gastro-enterostomy opening; j, jejunum; d, duodenum; p, pancreas; o, esophagus (natural size).

closure of the pylorus and his views are now almost universally accepted. A careful examination of the literature by one of us (Shaw) in 1904 revealed 117 cases while Ibrahim collected over 400 cases in 1908 and a

number of cases have been reported since then. This condition is therefore by no means uncommon and must frequently be overlooked.

Pfaundler found that the first vomiting or onset of the disease was between the fourth and fourteenth days in 50 per cent. of the cases, from the second to third week in 25 per cent., and from the third to sixth week in 25 per cent. Five out of nine of our cases started in the first and second weeks of life, two in the third week, one in the fourth and one after the fourth.

Boy babies are affected, according to Ibrahim, about four times as frequently as girls, but in our cases five of the nine were boys. Five of our nine were first-born babies and in two families subsequent children have shown no gastric disturbances. In one family the first child is strong and healthy, the second child died after an operation to relieve

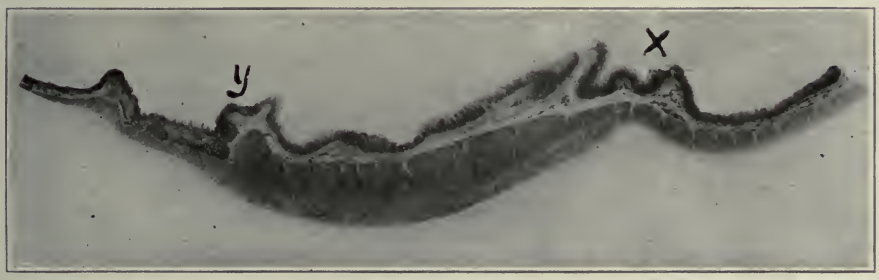


Fig. 6.—Case 4. Longitudinal section of wall of pyloric canal showing the greatly thickened muscular wall. The duodenal end of the "canal" is indicated by "y" and the gastric end by "x". These points are well marked, the former by the duodenal submucous or Brunner's glands, and the latter by a definite indentation; here the thickening of the muscle coat begins. Hematoxylin-eosin stain. (Mag. x 4.)

the stenosis (Case 3) and the third child died when 6 weeks old from a typical attack of this disease. This is the only instance among our cases in which there appeared to be any family tendency.

Nearly all the cases of pyloric stenosis occur in breast-fed infants, which is contrary to nearly all the affections of the digestive tract.

SYMPTOMS

A healthy and robust child in the first weeks of life is suddenly seized with violent *vomiting* without apparent cause. At first this occurs irregularly but later increases in frequency, often after each feeding. Examination of the breast milk shows it to be normal. Modifications of

cow's milk, changes in quantity or quality of the food or of the intervals of feeding have no effect on the vomiting. It is forceful and projectile and occurs suddenly without warning. It is variable in amount, and the quantity of fluid thrown up is surprising. The child will apparently retain several of its feedings but suddenly will throw up all the previous feedings. Six ounces may be thrown up in a jet-like explosion. The vomited matter consists of slightly digested milk mixed with mucus. It never contains bile.

This vomiting is not controlled by the usual medicinal remedies. Lavage may reduce the vomiting to once or twice a day. The tongue remains clear and the breath sweet.

Constipation and impaired nutrition are directly dependent on the vomiting. The constipation is really deficient defecation resulting from the diminished intake of food and fluid. Cases have been observed in which no bowel movement could be obtained for twelve days. The stools are small in amount, dark green, very offensive, and contain much mucus. The urine is scanty and high colored.

The *weight* of the infant is the index of his nutrition. The loss in weight in this disease can amount to 1 ounce or more a day. There is a progressive emaciation which is shown later by extreme exhaustion, subnormal temperature, depressed fontanel, sunken cheeks, etc.

The lower part of the *abdomen is flat* and even sunken in, while the upper part is distended and prominent. This gives the abdomen a characteristic appearance.

The most characteristic symptom and one that is pathognomonic of this condition is the *visible peristaltic contraction* of the stomach. This has been termed "stomach stiffening" and is due to the strong muscular contraction of the narrow pylorus. The stomach appears to stand up on itself. This is seen during sleep as well as when the child is awake. The wave starts from the left side and is about the size of a hen's egg. The protruding part is often surrounded by deep retraction in the abdominal wall. Before it disappears to the right another wave appears where the first started. Hour-glass contractions may occur owing to the two waves running close behind each other. This visible peristalsis apparently is not painful, which is not the case with spastic contraction of the pylorus with which it is often associated.

An equally characteristic and pathognomonic symptom is a *palpable enlargement of the pylorus.* This is not regularly present especially in early cases. The pylorus was markedly enlarged in all of our six patients

operated on, and in none of them could the pylorus be palpated through the abdominal wall.

Dilatation of the stomach is present in advanced cases depending on the degree and duration of obstruction but is absent in the early stages, as the food is ejected as soon as the stomach is overdistended. The stomach contents may be retained over several feedings and then ejected, showing that little or no food passes out of the stomach.

Several authors emphasize the presence of *hyperacidity*. The increased acidity may be due to hyperchlorhydria or an increase in fatty acids.

PATIENTS OPERATED ON

CASE 1.—E. S., first child, breast-fed from birth. Vomiting commenced about the third month; admitted to St. Margaret's December, 1902, aged 6 months; weight 15 pounds 8 ounces; uncontrollable vomiting, visible peristalsis, constipation. The symptoms continued despite treatment and there was a steady loss in weight. Operation (anterior gastro-enterostomy) at the Child's Hospital by

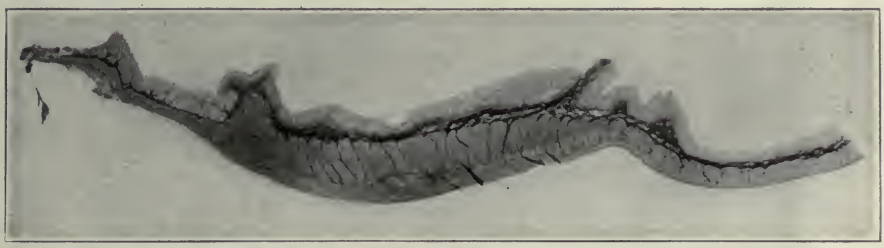


Fig. 7.—Case 4. Section same as Fig. 6, stained by Van Giesen's connective tissue stain. The large amount of muscle tissue is in marked contrast to the connective tissue which appears black. (Mag. x 4.)

Dr. Elting in June, 1903. Weight 12 pounds 1 ounce; "Stomach greatly dilated. pylorus firm and thickened, lumen greatly reduced and stenosis pronounced." No bile was ever detected in the vomitus before operation but was present afterwards.

The child made a good recovery and gained 9 pounds in five months, and is now a large, well-nourished girl without any stomach trouble.

CASE 2.—E. B. (referred by Dr. Pearson of Schenectady); first child; breast-fed. Vomiting commenced at the end of the first week and was projectile in character; visible peristalsis and constipation.

Operation (posterior gastro-enterostomy) by Dr. Elting, Nov. 23, 1906, when the child was three weeks old. Died Nov. 28, 1906. No post-mortem allowed. Operation protocol reads as follows:

"On opening the abdominal cavity, a large distended stomach ballooned out. The intestines were collapsed and appeared as mere ribbons. There was complete stenosis of the pylorus due to a tumor the size of a small pigeon's egg and regular in outline. It was impossible to force gas through at this point. After anastomosis the intestines began to dilate and fill with gas."

CASE 3.—M. M., referred by Dr. Maby of Mechanicsville; second child; first child was strong and healthy. This child was breast-fed and commenced vomiting at three weeks. It was admitted to St. Margaret's Nov. 1, 1909. There was visible peristalsis (Figs. 1, 2, 3). Vomiting was controlled by lavage, but the stomach retained all food. There was constipation. Weight at birth 7 pounds; at five weeks 5 pounds 14 ounces.

Operation (posterior gastro-enterostomy) by Dr. MacDonald, Nov. 4, 1909. Weight at that time 5 pounds 9 ounces. Child died Nov. 5, 1909; no post-mortem

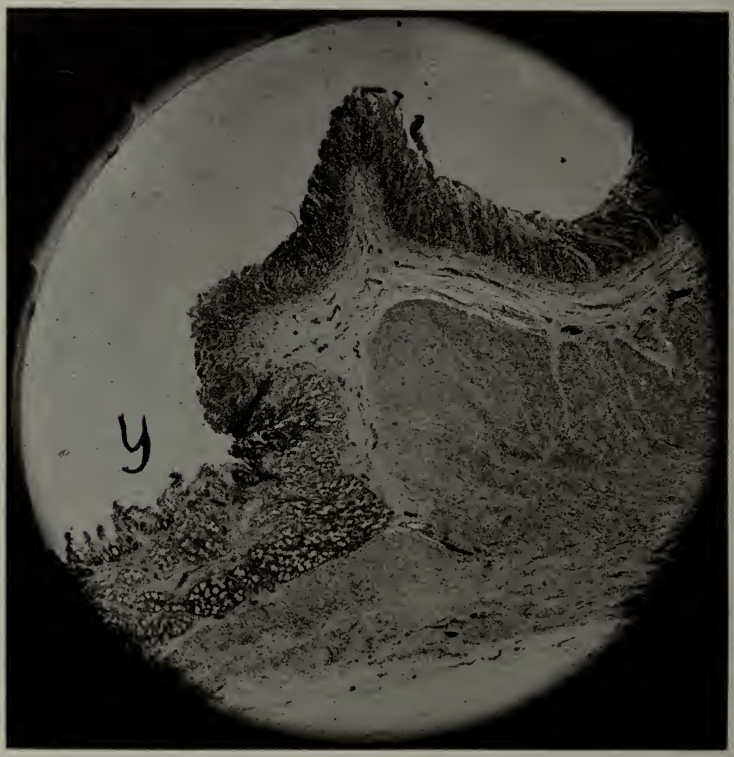


Fig. 8.—Case 4. Portion of Fig. 6 showing duodenal end of wall of pyloric canal. The submucous (or Brunner's) glands begin at "y," to the left is duodenum and to the right the pylorus. The thickness of the walls is in marked contrast. Minute black foci scattered through the submucosa, muscularis, and serosa indicate the inflammatory changes above referred to. (Mag. x 40.)

allowed. At the operation a firm tumor was found at the pylorus. The stomach was distended and the intestines collapsed.

A third child was born last September. Two weeks later it began to vomit. There was visible peristalsis and Dr. Maby wrote that it was a

typical case of hypertrophic pyloric stenosis. On account of their experience with the other child they would not permit an operation, and the child died in October when 6 weeks old.

CASE 4.—C. D.; referred by Dr. Kurth, Schenectady; first child was breast-fed; began vomiting at two weeks; admitted to St. Margaret's Jan. 8, 1910, when five weeks old; weight 7 pounds, 8 ounces. There was visible peristalsis and constipation.

Operation (posterior gastro-enterostomy) by Dr. Elting, Jan. 8, 1910. Weight 7 pounds 1 ounce: "Markedly dilated stomach with a definite hard and firm construction at the pylorus. There is comparatively complete obstruction." The

Fig. 9.—Case 4.. Transverse section of walls of pyloric canal showing the greatly thickened muscular coat. Hematoxylin and eosin stain. (Mag. x 6.)

child made a good recovery and was discharged Feb. 6, weighing 8 pounds, 9 ounces. Returned to hospital Feb. 24, with severe ileo-colitis. There was no vomiting. Died of exhaustion Feb. 28, aged two months, three weeks. Autopsy by Dr. Ordway (Figs. 4, 5, 6, 7, 8, 9, 10).

CASE 5.—T. K., referred by Dr. Shaw of Lansingburg. First child and breast-fed. Vomiting commenced on the tenth day. There was visible peristalsis and constipation. The child was admitted to St. Margaret's March 15, 1911, and weighed 7 pounds, 3 ounces, at three weeks. Weight at birth was 8½ pounds.

Operation (posterior gastro-enterostomy) by Dr. Elting, March 19. Weight 6 pounds, 12 ounces. Died March 21. No post-mortem allowed. At operation there was dilated stomach, collapsed intestines, and a large pyloric tumor.

CASE 6.—M. C., referred by Dr. Lamont of Catskill; second child; first was strong and healthy; child was breast-fed and began vomiting at two weeks. Weight at birth was said to be 8 pounds; child was weaned at three weeks and all methods of feeding were employed. There were visible peristalsis, constipation and vomiting. The emaciation was extreme.

Admitted to St. Margaret's April 17, 1911, at 8 weeks and weighed 5 pounds, 11 ounces. The vomiting was controlled by lavage but the entire previous feedings would be removed at the next lavage. The child lost 8 ounces in four days.

Operation (posterior gastro-enterostomy) April 21, by Dr. Elting. The operation showed dilated stomach, collapsed intestines and very large pylorus. The stomach was removed and sections prepared by Dr. Ordway (Figs. 11, 12, 13, 14, 15, 16, 17).

Fig. 10.—Case 4. Section same as Fig. 9 stained by Van Giesen's connective tissue stain. The large amount of muscle tissue is in marked contrast to the connective tissue which appears black. (Mag. x 6.)

CASE 7.—H. P., first child, was breast-fed for first three weeks. Vomiting commenced at second week. Weight at birth 7½ pounds. Admitted to St. Margaret's Aug. 21, 1906, when 6 weeks old and weighed 6 pounds, 14 ounces. There were visible peristalsis and constipation. The peristalsis was visible for several months and there was a palpable pylorus. Weight September 2, 6 pounds, 7 ounces. The child improved slowly. Lavage was given twice a day and the child was nourished by rectal nutrient enemata. Weight at discharge December 20, 1906, 9 pounds, 5 ounces. He is now a strong, healthy boy.

CASE 8.—R. C. was the second child and weighed at birth 7¾ pounds. He was breast-fed at first and later had a wet-nurse. Vomiting came on suddenly at four weeks. There were visible peristalsis and constipation. Lavage was

employed by the mother. The weight at six weeks was 6 pounds. The condition lasted five months, and the child is now apparently healthy and strong.

CASE 9.—E. G. was the second child. The first was strong and healthy. Breast-fed for eight months. Mixed feeding was begun at five months. Weight at birth was 8 pounds. Lowest weight was 5 pounds, 8 ounces.

Vomiting commenced at the third week. There were visible peristalsis and marked constipation. A pyloric tumor was very plainly felt. Weight at 9 months was 8 pounds, 11 ounces. The mother used lavage twice a day for several months.

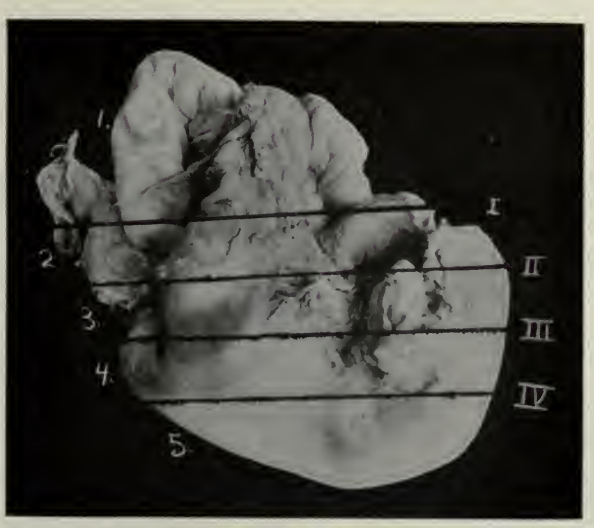


Fig. 11.—Case 6. Stomach, duodenum, and adjacent portion of small intestine of infant. The jejunum is sutured to the posterior wall of the stomach near the pylorus. I-IV indicate the location, and the plane of the sections which divide the specimen into five fragments (1-5) see Figs. 12 and 17 (5/7 natural size).

PATHOLOGY

Introduction

Secretion and digestion are often regarded as the most important functions of the stomach; absorption and assimilation, it is agreed, are chiefly performed elsewhere. We are apt to overlook the functions of storage and motility. The importance of these is emphasized in many animals; in the rat, for example, a large part of the stomach is lined by stratified squamous epithelium with a distinct horny layer, the secretory glands being situated in the small pyloric portion. The muscle coats are more evident at the pylorus. The circular muscles are usually distinct

and reach their maximum thickness just before the beginning of the duodenum. The oblique fibers are not so well defined and may merge into the circular or the longitudinal muscles.

Discussion of Pathological Findings

In these cases most writers describe a tumor occupying the position of the distal part of the pylorus. We shall designate this as the "pyloric canal," which connects the smaller funnel-shaped, or pyloric, portion of the stomach with the duodenum. The proximal end is indicated by a constriction (Fig. 6 x) and the distal by the duodenal submucous glands.

The tumor-like enlargement varies from 1.5 cm. to 3 cm. in length and 0.75 to 1.5 cm. in thickness. It is described by Scudder as a resilient

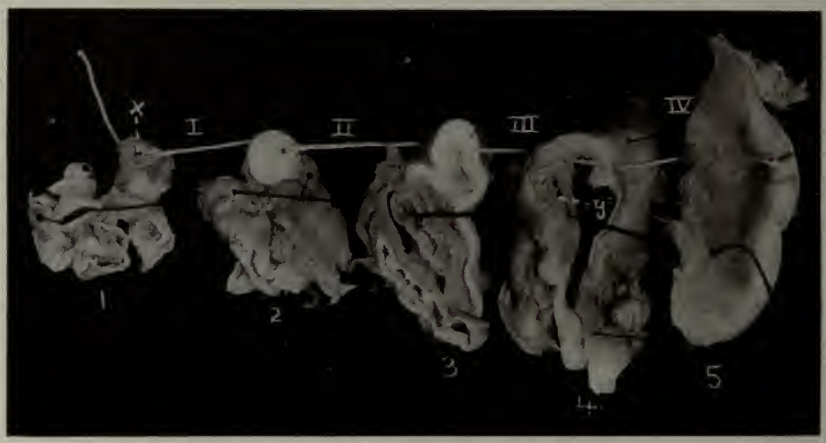


Fig. 12.—Case 6. Five sections showing four serial surfaces 1-I, 2-II, 3-III, 4-IV (see also Fig. 17). A white cord passes through the natural food channel, the walls of which at the pyloric portion of the stomach are greatly thickened (sections 2 and 3); the duodenum is of normal thickness (section I-"X"). A dark cord passes through the gastro-enterostomy opening (section 4-"y"), and indicates the course of the artificial food channel (½ natural size).

cylinder about the size of a hickory nut. Its consistency is very firm, so that Dilz speaks of it as a cartilaginous tube. The tumor is composed of the greatly thickened muscle coat of the "pyloric canal," chiefly of the inner or circular layer of fibers. Our measurements[1] in general agree with those of other observers. No difference was found in the length of the nuclei in the normal control case and in the two cases of hypertrophy

1. See table of measurements.

of the pylorus, although the thickness in the latter two was somewhat less. The caliber and patency of the lumen of the "pyloric canal" is variable and the measurements depend in part on the method by which the specimen is preserved. In Case 4 a tapering probe was gently inserted through the "canal" and where the least resistance was encountered, the circumference of the probe was found to be 1.3 cm. By a similar method Wolbach in one case found a lumen of 2 cm. in circumference. The canal in Case 4 was carefully packed with absorbent cotton and after hardening in 10 per cent. solution of liquor formaldehydi (formalin) the diameter of the lumen was 2 x 3 mm. In Case 6, on the other hand, the

Fig. 13.—Case 6, Section 4, surface 4-IV, showing large patent gastro-enterostomy opening at "x"; the outer surface of a portion of the pyloric thickening is seen at "y"; "z" indicates the esophageal opening (natural size).

specimen had been preserved in toto in 10 per cent. solution of liquor formaldehydi and the diameter of the lumen, which was practically obliterated by folds of mucosa, was 0.14 x 0.49 mm. A normal control hardened by slowly injecting through it and then immersing in 10 per cent. solution of liquor formaldehydi measured 4.0 x 4.9 mm. in diameter.

The test of functional patency by hydrostatic pressure is fallacious, for the redundant folds of mucous membrane may act as valves; these and the subsequent shrinkage due to the preserving fluid may give a false appearance of almost absolute impermeability to the pyloric canal. There

is little doubt, however, that the lumen is encroached on by the ridges or folds of mucosa projecting into it. In some cases the mucous membrane is hypertrophied.[2] Dilated, cystic and flattened glands with excess of mucus were noted by Wolbach. Our cases showed an occasional dilated gland, but not more marked than in control cases. Longitudinal folds or ridges project into the lumen of the pyloric canal. Case 4 showed three marked folds and Case 6, four; in the control there were two. Dilz describes three ridges of mucosa projecting into and completely occluding the lumen. Cervix-like projections of the mucosa similar to those bulging

Fig. 14.—Case 6, Section 3, surface 3-III, showing great thickening of the pyloric walls in the vicinity of "x". The walls of the cardiac portion of the stomach are of normal thickness (natural size).

toward the duodenum may also be found at the proximal end of the pyloric canal. They occur, though less marked, in normal cases. It is these folds and ridges which form the so-called "pyloric valve."

Various inflammatory changes of the pylorus have been described in these cases. Larkin believes there is an increase in connective tissue. Weill and Pelm consider the hyperplasia of the pyloric muscles secondary to an inflammatory process, while Fredet and Guillinot think that an

2. See measurements, Cases 4 and 5, table of measurements.

inflammatory swelling of the mucosa and spasm merely aggravate the stenosis.

In our cases, one, Case 4, showed, microscopically, moderate chronic and slight acute inflammatory changes in the mucous, muscle and serous coats; in Cases 6 and "X" (control) there was no evidence of inflammation of the walls of the pyloric canal. The stomach, in cases of pyloric stenosis in infants, has been described as larger than normal by some writers and others have found it smaller; its wall also in some cases is thinned and in others increased in thickness. In Case 4 the muscles of

Fig. 15.—Case 6, Section 2, surface 2-II, showing great thickening of the pyloric walls at "x". The jejunum is seen at "y" (natural size).

the stomach wall near the pyloric canal were 0.7 mm. and in the control 0.9 mm. in thickness.

The duodenum, when mentioned, has been regarded as normal. In our own cases the thickness of the muscle coat was 0.49 mm. in Cases 4 and 6 and in that of the control "X," 0.16 mm.; this, however, may be within normal limits.

AUTOPSY AND LABORATORY FINDINGS

CASE 4.—Post-mortem examination, Bender Laboratory A-10-17, by Dr. Ordway, for Dr. Shaw, at St. Margaret's House, Feb. 28, 1910, at 9:30 a. m.

C. D., aged 2 months and 3 weeks, 7 hours post-mortem.

Body is that of a fairly well developed, poorly nourished, emaciated male infant. Bony framework is everywhere prominent. Skin hangs in folds. Eyes are sunken. External orifices are negative. There is very slight lividity of dependent portions and no *rigor mortis*. The abdomen is prominent, slightly elevated above the level of the chest. In the median line between the ensiform and umbilicus there is a whitened linear scar 7 cm. in length. There is no edema. The axillary and inguinal glands are slightly enlarged, distinctly palpable; otherwise the superficial glands are negative.

Note.—Autopsy incision restricted to surgical incision above mentioned.

Peritoneal Cavity.—The right lobe of the liver, anteriorly, in the median line and the omental tissue are adherent to the inner aspect of the operative

Fig. 16.—Case 6, Section 1, surface 1-I, showing duodenum "x"; adjacent to the pylorus is the pancreas "p"; the other openings represent sections of the duodenum and coils of jejunum (natural size).

wound above described; otherwise the peritoneal cavity is normally smooth, moist, and glistening. The pleural and pericardial cavities, the heart, lungs, spleen, liver, pancreas, adrenals, kidneys, aorta and genital organs are normal.

Gastro-Intestinal Tract.—The upper portion of the cardiac end of the stomach to the left of the esophagus is adherent to the adjacent peritoneum of the diaphragm by delicate fibrous adhesions. The stomach is small, does not reach the umbilicus and is empty. Rugæ are prominent. The walls of the pylorus are greatly thickened for a distance of 2 cm., having the consistency of a firm, hyperplastic gland and forming a distinct ovoid tumor-mass in the region of the pylorus. This is in marked contrast to the walls of the duodenum, which are thin and collapsed, and to the walls of the cardiac portion of the stomach, which

are of normal thickness. A tapering probe is inserted through this thickened portion of the pylorus without difficulty until a point 1.3 cm. in circumference is reached; that is, the circumference of the pyloric opening after death, with practically no pressure, is 1.3 cm. On the posterior wall of the stomach 1.5 cm. below the pyloric opening, which is marked by protruding folds of mucous membrane, is a large opening into the jejunum; the latter is firmly adherent to the posterior wall of the stomach (Figs. 4 and 5. The diameter of this opening is 1.4 cm. Pressure on the gall-bladder causes yellowish fluid to exude into the duodenum from the ampulla. The small and large intestines contain a small amount of bright yellow, semi-solid material with numerous light yellowish shreds. Peyer's patches and solitary follicles are prominent. The intestines are markedly distended by gas.

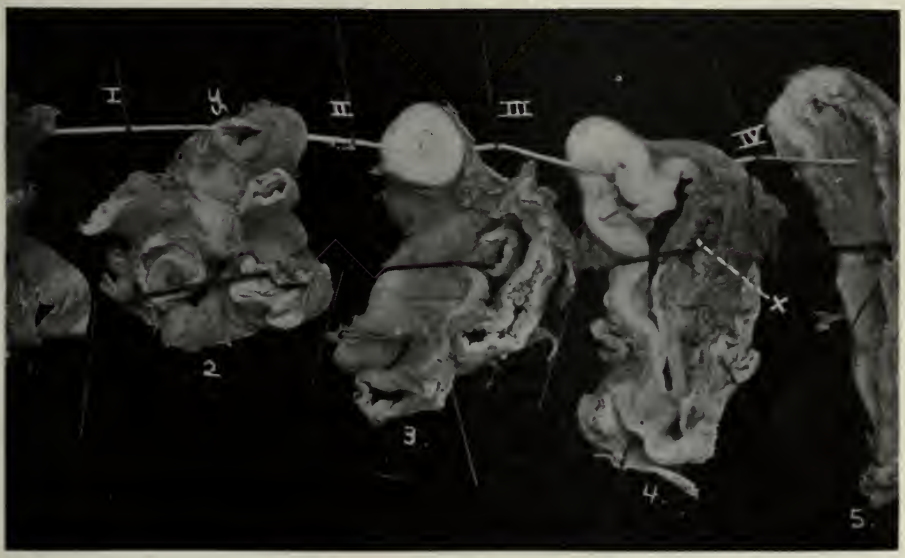


Fig. 17.—Case 6. Three sections and portions of two others showing three serial surfaces, 2-I, 3-II, 4-III. White cord passes through the natural food channel, the walls of which at the pyloric portion of the stomach are greatly thickened (3 and 4); the duodenum is of normal thickness (2 "y"). A dark cord passes through the gastro-enterostomy opening (4 "x") and indicates the course of the artificial food channel (5/7 natural size).

Note.—The surfaces here seen are the reverse of those shown in Figures 12 *et seq.*

Anatomic Diagnoses.—Emaciation, hypertrophy of pylorus, gastro-enterostomy; healed incised wound of abdominal wall, adhesions of omentum and liver to abdominal wall.

Microscopic Examination.—The stomach, duodenum and adherent jejunum are carefully filled with cotton saturated with 10 per cent. solution of liquor formaldehydi and these organs hardened in as nearly normal shape as possible. Particular care is taken that the stenosed pyloric and the artificial gastro-

enterostomy openings may be prevented from distortion by shrinkage (Figs. 4 and 5). Fragments removed from the wall of the "pyloric canal," as indicated in Figure 5, were cut in longitudinal and transverse sections and stained by hematoxylin and eosin and Van Giesen's connective tissue stains (Figs. 6 to 10). The great thickening of the wall is due to an increase in muscle tissue and chiefly to the circular fibers. There is slight atrophy of the glands in the mucosa and an increase in the interglandular tissue. An occasional gland is distended by lymphocytes and polymorphonuclear leukocytes. Scattered through the submucosa, muscularis and serosa, are numerous foci of lymphoid cells and few polymorphonuclear leukocytes; in many places similar cells distend the perivascular lymphatics. There is no increase in connective tissue. In the serosa there is a small amount of old yellowish pigment.[3]

CASE 6.—Michael C. Bender Laboratory, A-11-42. Post-mortem examination performed by Dr. Donhauser and restricted to surgical incision and examination of stomach, duodenum and jejunum.

Stomach, duodenum and portion of adjacent small intestine of an infant. The specimen was received in toto in 10 per cent. solution of liquor formaldehydi. It is somewhat shriveled by the preserving fluid and measures 7x5 cm. In the region of the pylorus is a hard tumor mass measuring 2x1.5 cm. The jejunum is sutured to the stomach on the posterior aspect near the pylorus (Fig. 11). Serial sections as indicated, I, II, III, IV, are made and divide the specimen into five fragments 1, 2, 3, 4, 5 (Fig. 12). A white cord passes through the natural food channel, the walls of which at the pyloric portion of the stomach are greatly thickened (Figs. 12, 14, 15, 17), sections 3 and 2. The wall of the duodenum is of normal thickness (Fig. 12, Section 1 "X", and Fig. 16).

A dark cord passes through the gastro-enterostomy opening and indicates the course of the artificial food channel (Figs. 12 and 17). The thickening of the pylorus is not abrupt on the stomach side, but involves almost the entire pyloric portion of the stomach and gradually increases in thickness as the duodenum is approached. At the junction of the duodenum, where the submucous (Brunner's) glands begin, this thickening is at a maximum and here ends abruptly. The gastro-enterostomy opening is large and the canal is patent. The intestine and stomach are firmly approximated and there is no leakage or suppuration.

Microscopic Examination.—Fragments removed from the thickened wall of the pyloric canal, cut in transverse and longitudinal section, and stained by hematoxylin and eosin, show no pathologic change other than the great increase in the thickness of the muscle coat, chiefly of the circular fibers. These fibers appear normal.[4]

CASE "X" (Control).—Post-mortem examination by Dr. Kellert. Bender Laboratory A-11-47. May 25, 1911. Name unknown. Female infant, 8 months old. Child died with cerebral symptoms. Examination restricted to chest and abdomen, all the organs of which appeared normal. Stomach and duodenum hardened by carefully injecting and then immersing in 10 per cent. solution of liquor formaldehydi. Fragments were removed from the wall of the apparently normal pyloric canal, sectioned transversely (Fig. 18) and longitudinally (Fig.

3. These inflammatory changes may have been secondary to the healing of the gastro-enterostomy wound. Patient 6 died before such change could have occurred.

4. See also table of measurements.

19,[5] and stained by hematoxylin and eosin. Microscopic examination reveals no pathologic changes. Although this child was 8 months old, it was taken as a control to Cases 4 and 6, which were, respectively, 11 weeks and 8 weeks; notwithstanding this great difference in the age, the walls of this normal pyloric canal, as shown in Figures 18 and 19, and as indicated in the table of measurements, are in striking contrast to those of the pyloric canals in the cases (4 and 6) of muscular hypertrophy of the pylorus.

TABLE OF MEASUREMENTS, CASES 4, 6, AND "X" (CONTROL)

	Case 4	Case 6	Case "X" (Control)
	mm.	mm.	mm.
Length of pyloric tumor "pyloric canal"	16	18	11
Thickness of tumor, external diameter	12	14	9
Thickness of muscle layers	2 to 3	3 to 3.5	1 to 1.6
Thickness of circular fibers	1.64	2.57	0.98
Thickness of oblique and longitudinal fibers	0.56	0.45	0.16
Diameter of lumen	3.0 x 2.0	0.49x0.14	4.9x4.0
Width of serosa	0.16	0.13	0.08
Thickness of mucosa and submucosa, from top of folds	1.8 to 3.5	3.5	2.0
Thickness of mucosa and submucosa, base of folds	1.06	1.1	0.82
Thickness of epithelium	0.41	0.90	0.49
*Mucosa, number of folds	3	4+	2+
Stomach, thickness of muscle coats near "pyloric canal"	0.7	—	0.9
Duodenum, thickness of muscle coats near pylorus	0.49	0.49	0.16
Muscle nuclei, width	1.9 to 2.5	2.0 to 2.5	3.8
Muscle nuclei, length	28 to 34	28 to 34	28 to 34

*When small irregularities are present as well as the distinct folds, they are indicated by + following the number of folds designated.

PATHOGENESIS

There are a number of theories and conjectures concerning the pathogenesis of this condition. The earlier writers considered it a congenital organic defect due to excess of development. Cautley claimed that this was a primary hypertrophy, an instance in which "Nature in her extreme anxiety to provide an efficient pyloric sphincter, has over-exerted herself, and produced too great an amount of muscular tissue."

Flynn considered it an atavistic deformity analogous to the gastric mill in insects and crustacea and the gizzard in birds, or a reversion to the edentate pylorus seen in the armadillo. The assumption that there was a true tumor has not been proved histologically.

---

5. Owing to a mistake in reproducing, Figures 6 and 7 were reduced from mag. x 6 to mag. x 4, while the "control," Fig. 19, was reduced from mag. x 6 to mag. x 5½. Because of this the contrast is not evident in these longitudinal sections, but is shown well when Figs. 9 and 10 are compared with Fig. 18.

The term "congenital" is misleading as no true hypertrophy has been found in fetal life or at birth. The symptoms rarely if ever appear before the end of the first week, which is irreconcilable with the hypothesis of a congenital obstacle.

Fig. 18.—Case "X" (Control).—Longitudinal section of wall of normal pyloric canal. Compare with Fig. 6 (Mag. x 5½).

Fig. 19.—Case "X" (Control).—Transverse section of wall of normal pyloric canal. Compare with Fig. 9 (Mag. x 6).

The later writers, as a result of the study of a large number of cases, are almost unanimous in the opinion that the hypertrophy or muscular hyperplasia is a secondary manifestation. This is the result of a spasm or incoordination of the gastric muscles. The spasm may start as a reflex spasm of the gastric mucosa incited by erosions, fissures, over-activity, hyperacidity, too high fat in the food, increased nervous irritability, etc.

Still has advanced an ingenious theory that the spasm is a kind of "stomach stuttering" in which the muscular action of both ends of the stomach is antagonistic. This he claims is analogous to the disturbance of coordination which is evident in hiccough or in the stuttering which is almost physiologic in the young child who is learning to talk.

Case 1 of our series shows conclusively that spasm of the pylorus will produce a marked hypertrophy.

COURSE

The course is slowly progressive and the condition may last from three to twenty months. The duration depends on the degree of stenosis. In cases in which recovery occurs the vomiting gradually subsides, constipation improves and the baby begins to gain in weight. This disease must be considered a very grave affection. Dr. John Thomson's statistics show that four children recovered out of seventeen treated medically, or a mortality of about 76 per cent., while eight recovered out of twenty-three treated surgically, or a mortality of 65 per cent. These figures are a little higher than those given by Ibrahim, who showed a mortality of 46 per cent. of patients treated medically and 54 per cent. surgically. In this connection it may be stated that successful surgical cases are more liable to see the light of publication than those resulting fatally.

DIAGNOSIS

The diagnosis is not difficult. The history, age of the child, visible peristalsis and other symptoms should at once arouse suspicion. In acute gastric conditions there is always more or less temperature and there is no constipation. It should not be mistaken for dyspepsia from overfeeding, or the habitual vomiting of Finkelstein, in which there is a congenital hyperplasia of the gastric mucosa. The latter condition is caused by too high fat in the food and the vomiting comes on immediately after feeding. True congenital malformations are rare. These are the result of an arrest in development or inflammatory process in fetal life. The baby only lives a few days after birth. The vomitus will contain bile if the obstruction is below the pylorus.

The condition most liable to be confounded is that of functional spasm of the pylorus or pylorospasm. Vomiting is the chief symptom in both these conditions, but in the simple spasm the stools are more frequent and bulky and the child may even have diarrhea. It occurs later in infancy and there is never any marked visible peristalsis and never any palpable pylorus. There may be bile in the vomitus at times.

TREATMENT

The treatment should be individual and each case must be studied intelligently.

The *dietetic* treatment consists in using the breast milk if possible. If the milk is rejected immediately after nursing, it might be pumped from the breast and given in small quantities with a medicine dropper. Some authors advocate giving it ice cold. If the breast milk contains too much fat it can be allowed to stand a few hours and the fat removed and the bottom milk given. Peptonized skimmed cow's milk will sometimes be retained. Whey, malt soup, albumin-water, acid-milk, etc., may also be tried. It is best to give small amounts at frequent intervals. Feeding by gavage should be employed.

The *mechanical* treatment is most important. Washing the stomach out several times a day with cold water removes the contents of the stomach and prevents fermentation and other changes and also tends to relax the muscles of the stomach. Any intelligent mother after a few lessons can perform lavage successfully. In two of our cases the mothers kept this up for many months without any difficulty. The use of hot compresses over the abdomen after feeding has also been recommended.

The *drug* treatment is unsatisfactory. Alkalies can be administered after feeding to reduce the acidity. The use of small doses of atropin, opium or cocain about half an hour before each feeding has been recommended by some authors.

Surgical treatment should be employed when no further good can be done by conservative methods. Surgery has added much to our knowledge of the pathology of this condition. There are several operations recommended to relieve this condition. A posterior gastro-enterostomy seems to be the choice of most surgeons.

SUMMARY AND CONCLUSIONS

1. The pyloric tumor is due to a thickening of the walls of that portion of the pylorus adjacent to the duodenum—the pyloric canal.

2. This thickening is caused by an hypertrophy of the muscle coat, chiefly the circular fibers.

3. The cause of this hypertrophy is not evident.

4. Inflammatory changes may or may not be present.

5. Spasm of the (hypertrophied) muscles, due to local or reflex cause, may be a factor in producing stenosis.

We are indebted to Dr. Ellis Kellert for assistance in the technical work and to Mr. J. A. Glenn for photomicrographs.

361 State Street—143 South Lake Avenue.

A DISCUSSION OF MIKULICZ' DISEASE, WITH REPORT OF A CASE OF LYMPHATIC LEUKEMIA IN A CHILD WITH MARKED ENLARGEMENT OF THE SALIVARY GLANDS

WILDER TILESTON, M.D.
NEW HAVEN, CONN.

In the year 1892 Mikulicz[1] described a new disease, characterized by chronic, bilateral, painless enlargement of the lacrimal and salivary glands. In the cases which formed the basis of his report the blood was normal and there was no involvement of the lymph-nodes or spleen. The histologic picture resembled that of a lymphoma. There was no tendency to recurrence after complete extirpation. Mikulicz considered the disease to be due to some inflammatory agent of unknown nature.

Since then, however, cases have been reported in which pseudoleukemia or leukemia was accompanied by a similar enlargement of the lacrimal and salivary glands, and v. Brunn[2] in 1905 was able to collect a series showing all gradations from the syndrome described by Mikulicz to pseudoleukemia and leukemia. The association with the last-named disease, however, is so rare that the following case seems worthy of record.

Lymphatic leukemia of the "aleukemic" type, in a child 2 years old; large tumors of both parotid and both submaxillary glands, lacrimal glands not involved; autopsy.

History.—G. H., born Oct. 13, 1903, entered the Children's Hospital, Boston, Aug. 30, 1905. The baby was well till April, 1905, when she had fever, ranging from 103 to 105 F., for a period of three or four weeks. About three weeks after the temperature became normal, the parotid glands began to swell. Tincture of iodin applied over the glands caused them to decrease in size until they were scarcely noticeable by August 1, but the swelling soon returned. Bunches in the neck appeared three months prior to admission. There had been diarrhea, off and on, for two months previous to admission. I saw the child in the outpatient department of the Children's Hospital, and sent her into the hospital in the service of Dr. J. L. Morse, to whom I owe thanks for the privilege of reporting the case.[3]

1. Mikulicz, J.: Beitr. z. Chir. Festschr. (Billroth), 1892, 610.
2. Von Brunn, M.: Beitr. z. klin. Chir., 1905, xlv, 225.
3. This case has been reported in brief by Dr. J. L. Morse: "The Anemias of Infancy," Jour. Am. Med. Assn., 1909, lii, 455, Case 17. (For the earlier history I am indebted to Dr. J. W. Clarke of Attleboro.)

Physical Examination.—The child was well developed and nourished and only slightly pale, and weighed 26¼ pounds. The appearance of the face was striking, resembling a very marked case of mumps. Palpation revealed a hard swelling of both parotid glands, about the size of hens' eggs. The skin over the tumors was not reddened nor adherent, there was no pain and no tenderness on pressure. A short distance in front of the parotid on each side was a hard mass the size of a marble. (Accessory parotid glands.) Both submaxillary glands showed similar swellings the size of walnuts. The lacrimal and sublingual glands were not enlarged. There was no exophthalmos. The tonsils were considerably increased in size, but without exudate or ulceration. The lymph-nodes in the neck, axillæ and groins were considerably enlarged. The examination of the chest was negative except for slight dulness over the upper part of the sternum. The liver reached from the fifth rib to 5 cm. below the costal margin in the nipple line; the surface was smooth and the edge hard and sharp. The spleen was much enlarged, reaching from the sixth rib to 5 cm. below the costal margin, the long diameter being 12.5 cm. On the outer side of the leg were several small ecchymoses. There was no edema and the signs of rickets were absent.

Urine: Acid; no albumin, sugar or casts, but many leukocytes.

Blood: August 30, red cells, 6,860,000; hemoglobin, 95 per cent., leukocytes, 14,700; small mononuclears, 50 per cent.; large mononuclears, 23 per cent.; polynuclear neutrophils, 25 per cent.; eosinophils, 1 per cent.; basophils, 1 per cent.; no poikilocytosis and no nucleated red cells. September 1, red cells, 6,188,000. September 12, leukocytes, 11,500; small mononuclears, 51 per cent.; large mononuclears, 26 per cent.; polynuclear neutrophils, 21 per cent.; basophils, 2 per cent. September 14, leukocytes, 6,700; small mononuclears, 23 per cent.; large mononuclears, 41 per cent.; polynuclear neutrophils, 36 per cent. The child was in very fair condition, with a slight fever, till September 14, when the temperature suddenly rose to 106 F., and she died the next day.

Autopsy.—(Dr. C. W. Duval.) There were dull purple spots on the thighs, upper arms and forehead, averaging 5 cm. in diameter. The parotid and submaxillary glands were much enlarged and firm. The cervical, mediastinal and mesentery lymph-nodes were considerably enlarged, ranging in size from that of peas to hazel-nuts. The thymus gland was greatly enlarged, measuring 8 cm. in its long diameter. The heart and lungs were not remarkable. The spleen was very large, measuring 18 by 7.5 cm.; it was firm and purplish red, and on section showed small grayish-white areas the size of a pinhead or less. The liver was enlarged and smooth and rather soft; on section mottled grayish-yellow and light red. The gastro-intestinal tract was normal. The kidneys were large, the capsule greatly thickened and showing considerable hemorrhage on its inner surface. On section the cortex was yellowish-white with many small hemorrhagic areas. Scharlach R showed a moderate amount of fat in the convoluted tubules.

Microscopic Examination.—(W. Tileston.) All sections were stained with eosin and methylene blue.

Salivary Glands: The parotid and the submaxillary glands presented identical appearances. The acini were widely separated by dense masses of cells of the lymphocytic series, which will be alluded to hereafter as lymphoid cells. The secretory cells appeared normal, except that they were crowded together so that no lumen was visible, suggesting compression. In places, especially near the capsule, there was a diffuse infiltration with lymphoid cells, and no gland cells were seen. The capsule was thickly infiltrated with lymphoid cells. The connective tissue septa appeared increased in thickness, but were poor in cells.

Lymph Nodes: Sections of three lymph-nodes all showed similar changes. There was a general overgrowth of lymphoid cells, obscuring the normal structure. Only a very few normal follicles could be found. There was a considerable number of large cells with pale pink protoplasm and large vesicular nuclei (endothelial

Fig. 1.—Photograph of author's case, showing the enlargement of the parotid and submaxillary glands.

cells). One section showed infiltration of the adjacent fat tissue with lymphoid cells.

Bone Marrow: The bone marrow of the sternum showed lymphoid infiltration. Further details are not available because the section was lost before it was carefully studied.

Thymus Gland: The thymus showed a general overgrowth of lymphoid cells. Hassal's corpuscles were apparently diminished in number.

Liver: The liver presented a remarkable degree of infiltration with lymphoid cells, involving the whole organ, but most marked about the portal vessels. This infiltration was mostly diffuse, but in places, especially in the portal spaces, there were large foci of lymphoid cells. Here and there a clump of these cells might be seen to lift up the endothelium of a central vein. In some places a blood-vessel was clearly separated by an endothelial wall from a mass of lymphoid cells; the latter, therefore, as Dr. Mallory pointed out to me, were situated in a lymph-sinus. The parenchymal cells were normal, except for some compression and atrophy.

Spleen: There was a striking infiltration with lymphoid cells along the larger vessels and next to the trabeculæ; the blood-sinuses were engorged with red cells. The follicles were enlarged, and some of them showed proliferation of endothelial cells at the center.

Kidneys: There was a high grade of lymphoid infiltration, both diffuse and circumscribed. A broad band of tissue in the cortex showed no trace of parenchyma, nothing but lymphoid cells, with a reticulum of fine connective tissue with capillaries. Elsewhere in the cortex there were strips of infiltration about the vessels, and parallel to the straight tubules, which were shoved widely apart. The parenchyma appeared normal.

The lungs, heart, stomach, intestine, ovary and urinary bladder all showed a moderate infiltration with lymphoid cells. The adrenal gland was normal.

The histologic picture was so typical that Dr. Mallory made the diagnosis of lymphatic leukemia without hesitation. There can be little question that this case should be classified as lymphatic leukemia of the "aleukemic" or "preleukemic" type; that is to say, without increase in the leukocyte count. The histologic appearance of the salivary glands. however, is identical with that described in many cases of Mikulicz' disease without involvement of the blood or lymphatic system, so that the case also fits in with the Mikulicz syndrome. The absence of enlargement of the lacrimal glands does not preclude such a classification, for although in the *typical* cases of Mikulicz' disease the lacrimals are involved, a number of instances have been reported in which they were not.

A search of the literature shows that the association of leukemia with the Mikulicz syndrome is extremely rare, only eight cases having or leukemia (eight out of twelve). The preponderance of females over males (eight out of twelve) may well be due to chance. Reuss[4] has

4. Von Reuss, A.: Jahrb. f. Kinderh., 1909, lxx, 161.

reported four cases of chronic relapsing parotitis in children, in which both sides were affected, but which differed from Mikulicz' disease in that there were acute exacerbations of an inflammatory character.

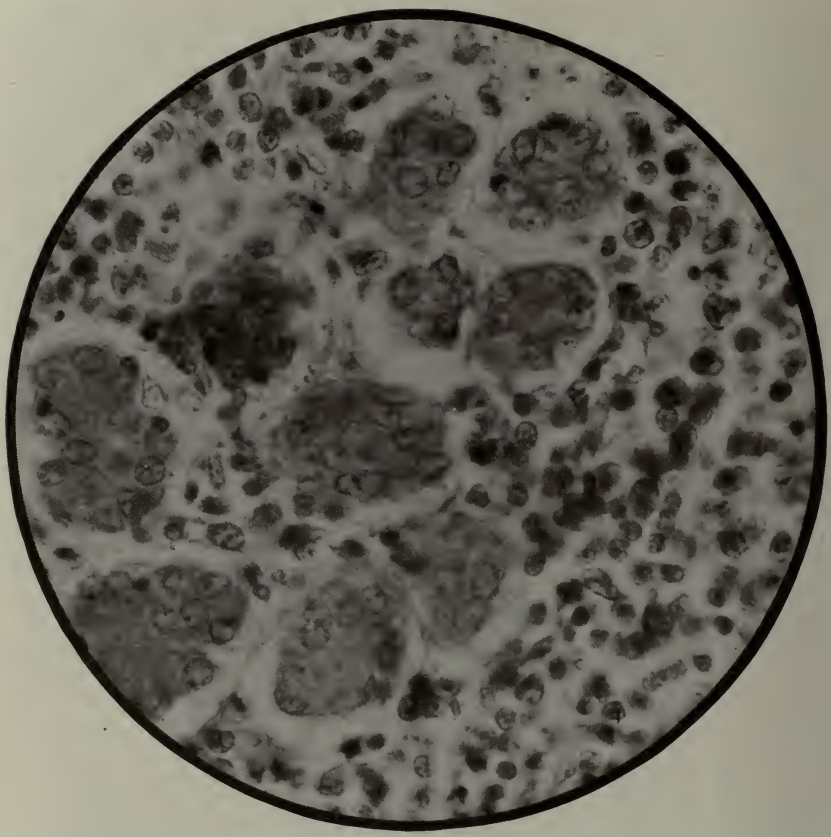


Fig. 2.—Photomicrograph of parotid gland, high power, showing acini and infiltration with lymphoid cells.

MIKULICZ' DISEASE IN CHILDREN

Up to the present time twelve cases of children showing the Mikulicz syndrome have been reported. The only striking difference from the disease as seen in adults is the large proportion with pseudoleukemia or leukemia (eight out of twelve). The preponderance of females over males (eight out of twelve) may well be due to chance. Reuss[4] has reported four cases of chronic relapsing parotitis in children, in which

both sides were affected, but which differed from Mikulicz' disease in that there were acute exacerbations of an inflammatory character.

CLASSIFICATION

The cases reported as Mikulicz' disease may be divided into three main groups as follows: 1. Those with involvement of the lacrimal and salivary glands in various combinations, but without changes in the blood, lymph-nodes or spleen; this is the Mikulicz' disease *par excellence.* 2. Those with enlargement of the lymph-nodes or spleen, or both. 3. Those with leukemia.

The first two groups are represented by numerous examples, while the third is a rare condition. Some of the cases in group two are probably to be considered as belonging to pseudoleukemia, especially those with very large spleens, with skin nodules, and with lymphomata in the intestine (Butterfield's case).[5]

ETIOLOGY

It is evident to anyone who studies the literature carefully that several different conditions have been described as Mikulicz' disease. Those cases showing leukemia or pseudoleukemia may be eliminated at once; they are simply unusual locations of the lymphomata common to these diseases. It should be emphasized, however, that a number of cases have been classed as pseudoleukemia without sufficient evidence; in many of them it is simply stated that the spleen and the lymph-nodes were increased in size, without mentioning the degree of the enlargement. Yet a moderate degree of enlargement of these structures is often met with in most of the chronic infectious diseases. The frequency of recovery in these cases (in Fleischer's[6] Case 1 the patient was well eight years later) is quite against the diagnosis of pseudoleukemia. One can find comparatively few out of the many cases with enlarged spleen and lymph-nodes in which the diagnosis of pseudoleukemia will bear a strict critique.

The interesting cases of simple hypertrophy of the salivary glands should also be excluded. This is a rare condition, described hitherto only by French observers. In two such cases (Jayle[7] and Frenkel[8])

5. Butterfield, E. E.: Physician and Surg., Detroit, 1907, xxix, 49.
6. Fleischer, B.: Klin. Monatsbl. f. Augenh., 1910, xlviii, 289.
7. Jayle: Bull. Soc. anat. d. Paris, 1894, 5 S. viii, 120.
8. Frenkel, H.: Arch. med. de Toulouse, 1909, xvi, 73.

tissue removed by incision showed normal structure. Apert's[9] case of dwarf growth in a man with enlargement of the parotids and breasts and glycosuria probably belongs in this class.

After these limitations there remains a considerable number of cases to which the term Mikulicz' disease may be more properly applied. They present the following features: chronic, painless and symmetrical enlargement of the salivary glands or lacrimal glands, or both, with or without moderate enlargement of the spleen and lymph-nodes; a benign course with no tendency to recurrence after complete extirpation of the affected glands; frequent cure under the use of arsenic, iodids or the *x*-ray, sometimes spontaneously.

For a part of the cases of Mikulicz' disease in this stricter sense, tuberculosis is the probable cause, as has been shown by Fleischer.[6] This observer reported four such cases, in two of which typical tubercles were found in the excised glands. The diagnosis was confirmed by Baumgarten. In one of these two the swellings of the salivary and lacrimal glands and a tuberculous iritis disappeared during a tuberculin cure. In none of the patients, however, were tubercle bacilli found in the glands. In Napp's[10] case, which was in other respects typical, miliary tubercles with caseation and tubercle bacilli were found in a bit of the conjunctiva which was excised. The ultimate proof, the demonstration of tubercle bacilli in the salivary or lacrimal glands themselves, still remains to be furnished, and it is possible that some cases taken to be tuberculosis were in reality instances of Hodgkin's disease of the Fischer-Reed type, which notoriously resembles tuberculosis.

Syphilis could be excluded in most cases and was the probable cause in only one, that of Gutmann,[11] in which a typical Mikulicz syndrome occurred three years after infection in a man who had previously shown the eruption of secondary syphilis; the administration of potassium iodid was followed by a cure, but no certain proof of the syphilitic nature of the Mikulicz syndrome was adduced.

For the remaining cases the etiology is obscure. The most likely cause seems to be some infectious agent in the widest sense of the word, as Mikulicz himself assumed. The possible modes of entrance are twofold; either by the ducts or by the blood current. In favor of the former are the facts that the lacrimal glands are almost always involved first,

9. Apert, E.: Bull. et. mém. Soc. méd. d. hôp de Paris, 1908, xxv, 155.
10. Napp, O.: Ztschr. f. Augenh., 1907, xvii, 513.
11. Gutmann: Berl. klin. Wchnschr., 1907, xliv, 1141.

and that in many instances there has been a previous or coincident inflammation of the conjunctiva. In favor of infection by the blood current is the bilateral character of the affection.

PATHOLOGIC ANATOMY AND HISTOLOGY

The affected glands are uniformly enlarged and hard, the normal markings lost. Microscopically two types may be distinguished: (1) the lymphomatous, in which the acini are pushed apart by dense masses of cells of the lymphoid series, and (2) the chronic inflammatory, in which in addition to lymphocytes there are granulation tissue, endothelial cells, often giant cells and eosinophils. The first type is somewhat the more common; the second includes cases which may have been tuberculosis, or possibly Hodgkin's disease.

THE SYMPTOMATOLOGY

There remains little to be added to what has been said already. Besides the glands already mentioned there is frequently involvement of other glands related to the lacrimal-salivary system, such as the accessory lacrimals, Krause's glands in the upper eye-lid, the Nuhn gland on the under surface of the tip of the tongue, and sometimes the mucous glands of the mouth. There are sometimes small nodules in the conjunctiva. There may be disturbance of the function of the affected glands, usually in the form of diminished secretion, so that the mouth is dry and the shedding of tears is impossible. In many cases, however, the function has not been interfered with. The general health is not impaired, except in those cases associated with pseudoleukemia or leukemia, and symptoms of inflammation are conspicuous by their absence.

DIFFERENTIAL DIAGNOSIS

The diagnosis of those cases showing the complete syndrome is easy. Mikulicz' disease is distinguished from *lymphosarcoma* by the more chronic course and by the (usual) absence of swelling of the regional lymph-nodes; from *primary tumors* by the fact that both sides are involved; from *pseudoleukemia* and *leukemia* by the course of the disease and the examination of the blood. From *chronic relapsing parotitis* it is differentiated by the absence of symptoms of inflammation, and from *simple hypertrophy* by the histologic appearances, and the presence of enlargement of the lacrimal glands. The fact that plumbism and iodism

may occasionally cause parotid swellings should be borne in mind; also the occasional persistence for a few months of the swelling due to mumps. The *acute* Mikulicz syndrome described by Snegireff[12] only lasts a few days or weeks, and hence leads to no difficulty.

PROGNOSIS

The prognosis as to life is good in the cases not complicated with leukemia or pseudoleukemia. These latter diseases, however, can be excluded only by observation of the patient and repeated blood examinations, so that the prognosis should be guarded at first. A disappearance of the glandular swellings is likely to occur under treatment, but rarely spontaneously. During the course of acute infectious diseases a diminution of the size of the glands has been noted frequently, but it is followed by an increase to the former size.

TREATMENT

In a number of cases, the use of potassium iodid or arsenic has been followed by recovery. When these were ineffectual, exposure to the *x*-ray has in all the reported cases (Pfeiffer,[13] Haenisch,[14] Ranzi,[15] Fittig[16]) led to a disappearance of the swellings; relapses occurred in Pfeiffer's case, but were readily overcome by further *x*-ray treatment. Histologic studies by Pfeiffer showed that the *x*-ray exposures caused a disappearance of the lymphoid tissue, which was replaced by fibrous connective tissue, as occurs on exposure of *normal* lymphoid tissue to these rays. Complete extirpation of the glands is not followed by recurrence, but it is out of the question in the case of parotid on account of the certainty of damage to the facial nerve.

CONCLUSIONS

1. The term Mikulicz' disease should be reserved for those cases of chronic, painless bilateral enlargement of the salivary and lacrimal glands in which pseudoleukemia and leukemia can be excluded.

2. The cases occurring in the last-named diseases should be classified as pseudoleukemia or leukemia with the Mikulicz syndrome.

---

12. Snegireff, K. W.: Klin. Monatsbl. f. Augenh., 1906, xliv,[2] 245.
13. Pfeiffer, C.: Beitr. z. klin. Chir., 1906, l, 145.
14. Haenisch, F.: Fortschr. a. d. Geb. d. Röntgenstrahlen, 1906-7, x, 291.
15. Ranzi, E.: Mitt. a. d. Grenzgeb. d. med. Chir., 1906, xvi, 554.
16. Fittig: Allg. med. Centr-Ztg., 1904, lxxiii, 606.

3. The cause of Mikulicz' disease is probably some infectious agent in the widest sense of the word. It is likely that a number of different organisms may cause the symptoms of the disease.

For the bibliography the reader is referred to a recent article by C. P. Howard.[17] This writer, however, includes some cases which hardly belong in this category; e. g., cases of simple hypertrophy of the parotid gland and cases of unilateral involvement of a single gland.

I am indebted to Prof. F. B. Mallory for valuable assistance in the histologic work.

308 Crown Street.

REFERENCES

In addition to those numbered in the text the following references are given:
Cases of Mikulicz Syndrome in Leukemia.
Bäch, S.: (Case 1), Ztschr. f. Augenh., 1899, i, 234.
Dunn, T. D.: Tr. Coll. Phys., Phila., 1893, xv, 103.
Gallasch, F.: Jahrb. f. Kinderh., 1874, vii, 82.
Kerschbaumer, R.: Arch. f. Ophth., 1895, xli, 99.
Senator, H.: Berl. klin. Wchnschr., 1907, xliv, 965.
Stock (Case Lorenz), klin. Monatsbl. f. Augenh., 1906, N. F., i, 328.
Tileston's case.
Cases of Mikulicz' Disease or Syndrome in Children.
Dunn, J.: Arch. Ophth., 1907, xxxvi, 52.
Haltenhoff: Ann. d'ocul., 1889, cii, 110.
Marcuse, P.: Berl. klin. Wchnschr., 1904, xli, 1205.
Meller, J.: (Case II), Klin. Monatsbl. f. Augenh., 1906, xliv, 177.
Osler, W.: Amer. Jour. Med. Sc., 1898, cxv, 27.

17. Howard, C. P.: Internat. Clin., 1909, 19 S., i, 30.

AMYOTONIA CONGENITA: A CLINICAL AND PATHOLOGICAL STUDY

J. P. CROZER GRIFFITH, M.D.
Clinical Professor of Diseases of Children in the University of Pennsylvania,
AND
WILLIAM G. SPILLER, M.D.
Professor of Neuropathology in the University of Pennsylvania
PHILADELPHIA

The disease called by Oppenheim[1] "myatonia congenita," but for which the term "amyotonia congenita" is rather to be preferred, as less liable to cause confusion, was first described only eleven years ago. Since that time it has continued to arouse much interest, although its nature and true position among diseases are still not well understood and the number of reported cases is not great.

It consists, in brief, as originally described by Oppenheim, of a flaccid paralysis, apparently congenital, most marked in the extremities, especially the lower, and varying in degree up to almost complete paralysis of the whole body. There is no actual atrophy visible; the sensation is not disturbed; the tendon reflexes are diminished or abolished; the electrical contractility is much diminished; the hypotonia is so great that there is unusual passive mobility at the joints, and in bad cases the child is unable to sit and the head falls loosely in any direction.

One of us (Griffith[2]), in reporting, in May, 1910, a new case, that of Charles K., was able to collect and detail in abstract form but forty-eight other instances which seemed properly to belong in this category. In this article a study of the symptoms and pathological findings in the reported cases was also made and a bibliography appended. Some years earlier one of us (Spiller[3]) had published a personal case with the post-mortem findings. This was the first case reported in this country, and the first with necropsy reported by anyone.

Since the publication of the history of Charles K., above referred to, the child died, and we were fortunate in securing an autopsy. This is the second case with autopsy occurring in America. It is our purpose in the present paper to analyze briefly the clinical data given in the reports

1. Monatsschr. f. Psychiat. u. Neurol., 1900, viii, 232.
2. Archiv f. Kinderhk., 1910, liv, 241; also Trans. Amer. Ped. Soc., 1910.
3. Univ. Penna. Med. Bull., 1905, xvii, 342.

of cases published since the writing of this article, so far as known to us, and to discuss the pathology of the disease in the light of the findings in our own cases and in those of others.

Among the cases to be considered here we include those of Ashby and of Moussous and Carles, referred to in a footnote, but not analyzed in the earlier publication.[4] In giving these and other abstracts we have pursued the method employed in this publication, numbering them in continued series with those there detailed, and discussing symptoms briefly; this clinical portion being by way of an appendix to our earlier study of forty-nine cases (Griffith).

CASE L.—Ashby.[5] Girl, aged 8 years; family history negative; dated from birth. In bed, almost completely paralyzed; all muscles extremely flabby and wasted, including those of the face, which has little expression; can barely move limbs; cannot sit; some difficulty in mastication; reflexes absent or feeble; electrical reactions normal; intelligence somewhat impaired. Improved slightly under treatment.

This case is in many respects anomalous, especially in the extreme wasting and the unimpaired electrical reactions.

CASE LI.—Moussous and Carles.[6] Girl, aged 4 years and 3 months; family history negative; dated from birth. Cannot walk; can move arms slightly and feebly; cannot sit erect or roll over; face seems a little inert; no apparent atrophy but muscles soft; electrical contractility lessened; no reaction of degeneration; intelligence a little diminished.

CASE LII.—Naish.[7] Boy, aged 4 years and 11 months; family history negative; dated from birth.

Examination.—Hypotonia of all muscles of the trunk and limbs, but especially of the upper limbs; sits, with kyphosis; stands and walks uncertainly; all movements weak; knee-jerk almost absent; electrical reactions diminished; great passive hypermobility; intelligence normal.

CASE LIII.—Openshaw.[8] Boy, aged 7 years and 6 months; could move arms and legs until measles at 18 months, since then no power in legs; never walked; power in arms diminished slightly, but can write legibly; sits, with lordosis; cannot hold head up; decided wasting of

4. Griffith, loc. cit.
5. Arch. of Pediat., 1910, xxviii, 363.
6. Arch. de Méd. des Enf., 1910, xiii, 472. From Jour. de Méd. de Bordeaux, 1909, No. 44, 697.
7. Proc. Royal Soc. Med., 1909-10, iii, Neurological Section, 95.
8. Ibid., Clinical Section, 39.

muscles in arms, nothing said about legs; knee-jerk absent; contracture at hips, knees, and ankles; passive hypermobility of elbows; intelligence normal. "The muscles of the legs reacted to faradic, and gave a brisk contraction with the constant current." Improved decidedly under treatment.

Biopsy of a portion of hamstring muscle showed "fatty infiltration: absence of cross-striation; irregular clefts with granular débris, with signs of regeneration in various parts."

The history as given leaves open some element of doubt regarding the diagnosis. It is not clearly stated whether the condition was congenital. The apparently sudden development, or rapid increase, of loss of power in the legs following measles, and the wasting in the arms are also not in accord with the usual picture of amyotonia congenita.

CASE LIV.—Zahorsky.[9] Boy, aged 2 years and 3 months; could not walk; knee-jerk diminished; no electrical contractility; "everything very flaccid." Improved somewhat.

The author designates this a case of myatonia, but the very meagre details given in the brief society report leave the important diagnostic symptoms unstated. Possibly a fuller account will appear elsewhere.

CASE LV.—Skoog.[10] Girl, aged 22 months; family history negative; could sit and support head at 6 months; never crawled or attempted to walk. Disease not noticed by parents until fourteenth month.

Examination.—Partial flaccid paralysis of arms and legs; all movements weak; cannot walk except a few steps when supported; holds head erect; sits, without kyphosis; possibly slight weakness in muscles of facial nerve; excessive hypermobility on passive movement; well nourished; muscles soft; tendon reflexes abolished; feeble galvanic and faradic response in some muscles, not in others; no reaction of degeneration.

Microscopic Examination of Muscle.—Small piece of gastrocnemius removed. A section from immediately beneath the muscle sheath contained no muscle bundles, all being substituted by fatty tissue. A deeper section contained some small, pale muscular tissue and much fat; "some muscle fibers in process of destruction, and seem ending in continuity with substituted connective tissue;" much fatty tissue between bundles; no hypertrophied fibers; all quite uniformly atrophied; great nuclear proliferation. Blood-vessels have greatly thickened walls.

---

9. Amer. Jour. Obstet., 1910, lxii, 1132.
10. Jour. Amer. Med. Assoc., 1910, lv, 364.

The history of this case leaves some doubt about its exact nature. Strongly against the diagnosis of congenital amyotonia is the absence of a positive history of congenital origin. This makes it seem possible that the disordered condition developed later and had been an advancing one. On the other hand, more careful observation by the parents might have thrown a different light on the case.

Case LVI.—Hummell.[11] Boy, aged 3 years; family history negative; dated from birth; never crawled or walked. Cannot stand; sits, with kyphosis; head falls forward when fatigued; moves legs, although feebly; upper extremities involved, but less so; decided passive hypermobility; muscles soft; tendon reflexes abolished; slight diminution of galvanic and great diminution of faradic contractility; no reaction of degeneration; no contracture. Ten months later there was decided improvement and he could stand with assistance.

Case LVII.—Chéné.[12] Girl, aged 6 months; family history negative; fetal movements felt; paralysis noticed by mother at end of second month, but disease probably congenital.

Examination.—General flaccid paralysis; head falls any direction; kyphosis; cranial nerve supply normal; slight movements of hands and feet; limbs of normal size, but muscles feel soft, and fatty cutaneous tissue prevents determination of actual atrophy; extreme passive hypermobility of joints; knee-jerk and ankle-jerk absent; sensation and intellect normal; faradic contractility much diminished; galvanic response only with 10 milliampères.

Case LVIII.—Chéné,[13] second case (unpublished case under care of Comby). Boy, aged 10 months; family history negative; dated from birth. General feebleness of musculature; head supported with difficulty; moves limbs while lying in bed but ceases when lifted up; has difficulty in keeping himself erect when held on nurse's arm; muscles soft, no positive atrophy; no paralysis or contracture; knee-jerk diminished; passive hypermobility of ankles. Very large fontanelle and thorax flattened at the sides; rachitic rosary. In two months improved very greatly; could stand holding to objects; could hold objects in hands; knee-jerk present.

This case was carefully observed by a physician (Comby) with experience in this disease, and is doubtless a genuine one. The report, however,

11. Jour. Nerv. and Ment. Dis., 1910, xxxviii, 749.
12. Thèse de Paris, 1910.
13. Ibid.

does not make it clear that decided, early rickets was not a factor of importance.

Chéné, in his list of cases, included one reported by Gayarre,[14] of which we have not seen the original report, but from the brief extract given the case hardly appears to belong here, inasmuch as exaggerated reflexes and clonus were prominent symptoms.

CASE LIX.—Pollak.[15] Boy, aged 6 months, family history negative; fetal movements felt; dated from birth; arms and legs affected at first, but arms have improved somewhat.

Examination.—Head falls to side as in new-born; marked kyphosis; respiration entirely abdominal; tone of abdominal muscles diminished; upper and lower extremities show flaccid paralysis; arms and toes move slightly on strong stimulation; muscles soft, not surely atrophied, as fat covering is well developed and prevents examination; movements of muscles supplied by facial nerves decidedly diminished, as seen when child cries; sucks with little power; muscles supplied by hypoglossal nerves much involved, and tongue can be depressed by finger with great ease; great passive hypermobility of joints; tendon reflexes absent; no electrical reaction of muscles or nerves obtained; sensation normal. Improved decidedly in course of a month, but died three months later of "capillary bronchitis." Thymus found enlarged. Later report of autopsy to follow.

CASE LX.—Variot and Chatelin.[16] Girl, aged 3½ years; family history negative; symptoms noted at 6 months; said to have been worse at 2 years than when reported.

Examination.—Can make different movements with legs, but feebly; upper extremities involved but to less extent; sits, with kyphosis; cannot stand; holds head erect; passive hypermobility; thoracic movements normal; muscles soft without evident atrophy; tendon reflexes abolished; slight contracture at hip; faradic contractility almost abolished, galvanic much diminished; slight suspicion of degenerative reaction, but probably not genuine; intelligence normal.

The almost certain congenital origin and the decided improvement make this a well-marked case, the positive reaction of degeneration not being certain enough to become an element of doubt.

Eleven additional cases, of which the abstracts have been here given, possibly belonging to the category of amyotonia congenita, have, therefore,

14. Revista Clin. de Madrid, June 15, 1909.
15. Archiv. f. Kinderh., 1910, liii, 373.
16. Rev. Neurologique, 1911, xix, 138.

come to our notice since the report of Charles K:, and the analysis of other cases reported up to that date. This does not include two cases referred to by Cassirer,[17] of which we have no details. The cases vary in severity, and agree in the main with the general symptom complex of the disease. Inheritance of any family predisposition was not mentioned in any of them. In all, the disease began at an early age, the symptoms dating clearly from birth in the majority, and probably so in Chéné's first case. In Skoog's patient the symptoms were first noticed at 14 months, and in Variot and Chatelin's not until 6 months. This may be through failure of careful observation on the part of the parents. In the cases of Openshaw and of Zahorsky the reports do not make the matter clear. In Openshaw's case the occurrence of an acute disease (measles) certainly made the weakness worse at 18 months, if it had existed previously, while in Chéné's second case the process of recovery from the well-marked rachitis may have some bearing, to an extent not clear, on the unusual and rapid improvement in the symptoms exhibited.

Muscular hypotonia was present in the lower extremities in all the eleven cases. Walking unaided was impossible except in Naish's case. In some cases, of course, the early age of the patient at the time the report was made precluded the possibility of walking in any event. The arms were more or less involved in all cases, but generally less than the lower extremities, as far as data are given on this point. Only in the case of Naish was the trouble greater in the upper extremities. In Openshaw's patient there appeared to have been very little affection of the arms.

When sitting was possible, as it was in about half the cases, spinal curvature was liable to appear. The face is reported involved in the cases of Ashby (little expression), Moussous and Carles (a little inert), Skoog (possibly slight weakness), and Pollak (decided diminution of motion, with involvement of the hypoglossal nerve). This is an unusual proportion in comparison with that generally reported, involvement of the cranial nerves being uncommon. Interference with thoracic respiration is mentioned by Pollak only. Decided hypermobility on passive movement is referred to in nine cases. In the other two cases (Ashby and Zahorsky) no reference is made to the matter. No certain wasting of muscles was discovered, except in the cases reported by Openshaw and Ashby, but it is often stated that although the limbs seemed properly rounded, they were evidently soft, and the presence of the fat layer prevented the existence of atrophy being determined. The patellar reflexes were absent or greatly

17. Handb. der Neurol., Lewandowsky, 1911. ii.

diminished in all cases except that of Moussous and Carles' patient. The original of their publication was not accessible to us, but at least no reference was made to it in the abstract. The electrical reactions were diminished in eight of the eleven cases. In Chéné's second patient no reference is made to them; in Ashby's patient they were found normal,

Fig. 1.—Photograph of Charles K.

Fig. 2.—Photograph of Charles K.

this case being anomalous in that as in other respects; and in Openshaw's case there would appear to have been no diminution, but the matter is not quite clear. A suspicion of a degenerative reaction was found in Variot and Chatelin's patient, but the condition was considered not a genuine

instance of it. Some diminution of intelligence was reported by Ashby and by Moussous and Carles, but was evidently not of moment, and must be considered accidental, or apparent only. Contracture was present in the cases of Openshaw and of Variot and Chatelin. More or less improvement is said to have taken place in seven instances. In Ashby's and Zahorsky's patients it was slight; in Openshaw's, Hummell's, Pollak's, and Variot and Chatelin's it was decided; in Chéné's second patient it was so great that it appeared to be largely due to improvement in the rachitis present. Only one death was reported (that of Pollak's patient) due to respiratory involvement, as has so often been the case in this disease. This was the cause of the fatal ending in our patient, Charles K.

The history of Charles K. up to the last notes made at the time of reporting is, in abstract, as follows:

Boy, aged 15 months; admitted to the Hospital of the University of Pennsylvania, Dec. 8, 1909. Parents, drunkards. Child had general flaccid paralysis from birth, and had never been able to use his legs or handle objects. Examination showed inability to sit or (Figs. 1 and 2) to hold his head erect; only very slight movement of arms and legs possible; diminished expansion of the thorax; no rickets, no wasting of the limbs; knee-jerk absent; moderate passive hypermobility of joints; slight contracture; entire failure of faradic and galvanic response. Under treatment up to April 26, 1910, the child improved considerably.

The later history of the child reads: During the month of May, 1910, the boy had more or less fever; there was decided improvement in the ability to hold the head erect, but he could sit only when propped with pillows. The abdominal reflexes were absent; respiration was still almost entirely abdominal; the slight contracture previously mentioned persisted. Anemia was decided, and this, with irregular temperature, continued until July. He was then sent to the seashore, but returned in September in about the same condition as when he left the hospital. Little change of any sort took place, and there was certainly no improvement from this time. About the end of October, 1910, he developed bronchitis, with fever, then pneumonia, and died after an illness of five days.

The autopsy was performed by Dr. B. S. Veeder, and his report and our findings in the nervous and muscular tissues are the basis for the statements which follow:

General.—Body of a white male infant, about 2 years of age. The body was well nourished; no emaciation present; post-mortem rigidity absent; practically no lividity; no scars or external markings. The skin

was very pale, soft, and delicate in texture; no enlargement of the superficial lymphatics present; fontanelles closed. The autopsy was performed at a private house, under circumstances which made several features rather unsatisfactory.

Incisions were made in order to obtain nervous and muscular tissue. On incision of the calf the subcutaneous fat was found markedly increased, and measured 1.5 cm. in thickness; the blood-vessels showed as pale white cords; the muscle tissue markedly atrophic, being rather tendinous in character, of a very pale color, and soft and flabby in consistency. A similar condition was found in the forearm, where the muscle surrounding the bone was simply a thin layer about one-eighth inch in thickness. the rest of the arm, which was of about normal size for the age of the child, being made up of adipose tissue.

Abdomen.—On opening the abdominal cavity the fascia and subcutaneous tissue were found thickly infiltrated with a large amount of adipose tissue; the abdominal muscles little more than a thin sheath of tissue; the intestines distended, pale white, glistening in color, without adhesions; the liver extended slightly below the costal margin; no fluid present in the abdominal cavity. The abdominal wall showed a slight greenish discoloration of putrefactive change.

The spleen was moderately firm in consistency; maintained its shape when laid on a flat surface; weight, 26 grams; sharp edges, rather pale red in color, smooth capsule, measured 7.5 x 4 x 2.5 cm. The cut surface was rather pale, not very moist, bled slightly, and showed faint markings of trabeculæ and follicles.

The liver was of firm consistency, with sharp edges, smooth capsule, of pale reddish-brown color, weighed 460 grams, and measured 18 x 11 x 5 cm.

The pancreas was dark purple in color, of normal consistency, and 8.5 cm. in length.

The stomach was decidedly distended, the mucosa thin, rather atrophic, grayish in color; covered with considerable mucus, and without ulceration.

A small portion of the ileum was removed for microscopic study, but only the duodenum was examined in its extent. This showed a thin wall, with the mucous membrane slightly grayish in color and without ulceration.

The right kidney weighed 70 grams and measured 10 x 4 x 3 cm.; was firm, rather bulging, and cut with normal resistency. The cut surface was smooth, and showed slight thickening and overgrowth of the cortical

portion, which was pale white, and stood out in marked contrast to the dark red, congested pyramids. Throughout the kidney there were numerous small, grayish-white points, particularly in the pyramids and in the pelvic portion. The glomeruli were not visible. The vessels of the cortex showed distinct striation.

The adrenals were small, pale, and distinctly yellow in color.

The mesenteric lymph nodes were about the size of split peas; those of the retroperitoneum were not enlarged.

Thorax.—Both pleural cavities were free from adhesions, but a few adhesions bound together the lobes of the right lung. The pericardial sac was free from adhesions or fluid. The lower lobe and almost the entire upper lobe of the left lung were moist, dark blue in color, and firm; the rest of the lung exceedingly pale and crepitant throughout. The pleural surface showed markings of the alveolæ. Section of the dense firm area showed a deep blue, almost cyanotic color; the surface moist and exuding on pressure small white plaques of purulent material, with very slight bleeding. Section of the pale, soft, crepitant areas showed a rather normal appearance, except for quite marked anemia. The right lung weighed 180 grams; both the upper and lower lobes were involved in a bronchopneumonic process similar to that described in the other lung. The middle lobe was uninvolved.

The heart weighed 80 grams. The small, white, firmly contracted chambers contained small, firm, currant-jelly clots attached to the papillary muscles. The right ventricle contained soft clots in addition. The valves and orifices were normal in appearance. The musculature of the heart was rather pale, yellowish-gray in color, and of fairly good consistency. The papillary muscles, especially on the right side, were pale and short. The wall of the left ventricle measured 9 mm., and that of the right ventricle 3 mm. in thickness.

The aorta and blood-vessels exhibited no lesions.

The thymus gland was rather small, and extended downward beneath the sternum as far as the second interspace.

The thyroid gland was exceedingly small.

Nervous System.—No excess of fluid was found within the skull. The brain substance was soft and the membranes somewhat congested.

The spinal cord exhibited a rather edematous appearance of the membranes, with some coagulated blood extending almost the entire length of the canal.

The following tissues were prepared for histological examination: heart, lungs, liver, pancreas, kidney, adrenal, small intestine, thymus, thyroid, voluntary muscle, brain, cord, and nerves.

Heart: The cut surface showed a normal pericardium and endocardium. The muscle-fibers lay closely together, and both longitudinal and cross-striation were distinct. There was a slight granular condition of the protoplasm present. The nuclei were regular and oval in shape, and with considerable polar pigment. The blood-vessels throughout were filled with erythrocytes.

Lungs: Sections taken from the non-consolidated portion showed a moderate amount of congestion of the alveolar walls with occasional areas of edematous material partially filling the alveolar spaces. Sections from the consolidated part of the lung showed large areas in which the alveolar spaces were filled completely with an exudate consisting of leukocytes and broken-down cellular material. In most of these areas several bronchi could be made out in which there was almost complete desquamation of the epithelium, and the lumen filled with broken-down and disintegrated cells, and with leukocytes. Occasionally areas were seen in which the alveolar spaces were only partially filled and in which some air was still present. There was marked congestion throughout.

Liver: The capsule was normal, and there was no increase in the perilobular connective tissue. The central veins were empty, and only a few capillaries were injected. Throughout the entire lobule the liver cells contained large vacuoles, occasionally forming quite typical seal-ring cells. The lumen of the larger bile ducts was filled with faintly staining granular material.

Pancreas: The interstitial and periductal connective tissue was not increased in amount. The cells of the acini stained well and did not show degeneration. The islands of Langerhans were numerous anl large and showed nothing abnormal.

Kidney: The capsule was thin and regular. There was no increase in interstitial tissue in any part of the kidney. The cells lining the convoluted tubules stained poorly, and appeared as if smeared with eosin. The protoplasm was slightly granular and cell outline very indistinct. The nuclei were small and regular, and were rather solid, and there had been no loss of nuclei. The free margins of the cells were slightly irregular, and encroached somewhat on the lumen of the tubules. The capillaries between the tubules contained few erythrocytes. The glomeruli were large, and almost completely filled the spaces. There was no exudate in

the spaces, nor were there any evidences of proliferation present. The nuclei of the tufts were numerous and densely packed together, as is usually found in a young kidney. The blood-vessels of the tufts were well injected. Throughout the section marked congestion was seen.

All of the changes were explainable by a condition of post-mortem degeneration, but as the other organs did not show this to such a degree, it is possible that there had been a cloudy swelling present.

Adrenal: The capsule and interstitial tissue showed no abnormality. In the cortex the three zones were distinct. The medullary portion was compact, and contained several large blood-vessels with a clear lumen. The nuclei of the cortical cells were large and somewhat vesicular, and stained deeply. The protoplasm was highly granular and stained rather faintly, but the large vesicles so frequently seen were not present. The only noteworthy feature of the medullary portion was the absence of cells bearing chromatin pigment.

Small Intestine: The mucosa of the duodenum was in a decided state of post-mortem degeneration. The submucosa showed marked hyperplasia of Brunner's glands, which in places composed over half the entire thickness of the intestinal wall. The cells of the glands were granular and somewhat disintegrated. The other layers showed nothing abnormal. The ileum showed likewise considerable post-mortem degeneration of the mucosa, without other changes of note in the section.

Thymus: The thymus had undergone but little involution, the fibrous tissue between the lobules not being marked. The lobules were densely packed with cells. These were chiefly small, deeply staining lymphocytes, but numerous large cells, with oval and vesicular nuclei, were present. The corpuscles of Hassal were not very numerous, and were not fully developed. In many places there were small collections of the larger cells noted in which the cells were beginning to group themselves in a concentric manner, and transitions from this stage to a quite typical Hassal's corpuscle could be distinguished. Numerous eosinophilic cells were present, and these showed some slight tendency to occur in groups. There was a marked congestion of the blood-vessels.

Thyroid: The thyroid showed nothing distinctly abnormal. In a few places there was a slight hyperplasia of the epithelial cells lining the acini, and although the acini were uniformly filled with considerable colloid material, there was no dilatation of them.

The gross anatomical diagnosis consisted then of atrophy of the muscles, with general fatty infiltration; bronchopneumonia; cloudy swell-

ing and congestion of the kidneys, and slight cloudy swelling of the liver. The histological diagnosis, not including the muscular and nervous system, was bronchopneumonia, cloudy swelling of the kidney, and fatty infiltration of the liver.

As special interest attached to the condition of the muscular and nervous systems, we have given particular attention to this part of the pathological findings, with the following results:

The brain was unusually large, and appeared more like the brain of an adult than that of a child. It weighed 1,542 grams after it had been one week in a 10 per cent. formalin solution. The cord measured 23 cm. in length, and as it had been removed close to the foramen magnum, the difference in the relative size of the brain and cord was striking. The posterior spinal roots appeared to be of good size, and a transverse section of the cord was not unusually small. The anterior roots throughout the cord were small.

The cells of Betz in the right and left paracentral lobules were numerous, especially in the left, although no significance is to be attributed to this apparent excess on the left side. In some of the Betz cells the chromophilic elements were in normal form; in others they had become granular. The cells of the hypoglossus nuclei may have been a little diminished in number, but there was no noteworthy atrophy comparable with that of the cells of the anterior horns of the spinal cord.

Sections from the seventh and eighth cervical segments showed few nerve cells in the anterior horns, except that in the eighth cervical segment a group of cells was present on each side corresponding to the intermediolateral tract. The few cells remaining in the anterior horns were small, but contained chromophilic elements. No degeneration in the white matter was detected by the Weigert hematoxylin stain. The anterior horns by this stain appeared a little pale, as from a scarcity of nerve fibers.

The seventh and eighth posterior cervical roots, cut separately from the cord, were in excellent condition, showing no degeneration. The anterior roots from these levels were degenerated, but somewhat less so than the anterior roots of the lumbar region. No evidence of degeneration by the Marchi stain could be found in sections from the cervical, thoracic, or lumbar region.

The anterior horns of the lumbar region were paler than the posterior horns. The nerve cells of the anterior horns were few, and most of those present were shrivelled. The cells of Clarke's columns were in good

condition; some showed alteration — namely, chromatolysis and peripheral displacement of the nucleus — but such findings are not unusual in the cells of these columns.

The nerve cells of the anterior horns in the lumbar region did not show any noteworthy change by the Bielschowsky method. The first, second, and third anterior lumbar roots, cut separately from the cord and stained by the Weigert hematoxylin method, showed great diminution in the number of medullated fibers, and a considerable overgrowth of connective tissue was evident when acid fuchsin and hemalum were used for staining.

The first, second, and third posterior lumbar roots appeared to be normal. The difference between the anterior and the posterior lumbar roots was very striking, as the former were much degenerated.

Portions of muscle were taken from the back near the neck, from the forearm just below the elbow, and from the calf. The muscle from the forearm showed great atrophy of muscle fibers, but even these greatly atrophied fibers preserved their transverse striation, although longitudinal striation was not distinct. The atrophy affected certain bundles, and other bundles in the immediate vicinity in large measure escaped. The intramuscular nerve fibers stained by the Weigert hematoxylin method showed considerable degeneration, and in some nerve fibers the medullary substance appeared as broken into small black balls. Here and there in transverse section a bundle of rounded, unusually large muscle fibers was found. The atrophied fibers showed an excessive number of sarcolemma nuclei, in some places the nuclei forming dense masses, and almost obscuring the greatly atrophied muscle fibers. By careful examination the atrophied muscle fibers usually could be detected. The interstitial tissue was considerably increased. Some of the muscle fibers showed fatty changes within them by the Marchi method, in the form of minute droplets in small points.

Muscle from the back resembled that from the forearm, but was in better preservation; that is, the atrophy was not so intense. There were many highly congested blood-vessels. Marchi's method revealed fatty degeneration within the muscle fibers, but not so much as in the muscle from the forearm. Intramuscular nerve fibers stained by the Weigert hematoxylin method appeared partially degenerated. Some large muscle fibers were found. Many muscle fibers appeared rounded in transverse section. Some muscle bundles were little affected, and yet were surrounded by bundles of greatly degenerated muscle fibers.

The calf muscle was similar to that from the forearm, but the changes were more intense in the former. The muscle fibers were more atrophied, and the interstitial fibrous tissue was much increased in amount. The connective tissue nuclei were distinctly more numerous. Fatty change was evident by the Marchi method within many of the muscle fibers. There was an excessive amount of fat between them. A piece of nerve, probably the posterior tibial, cut with the muscle, showed much degeneration by the Weigert hematoxylin method. Intramuscular nerve fibers were considerably degenerated. The muscle fibers within the muscle

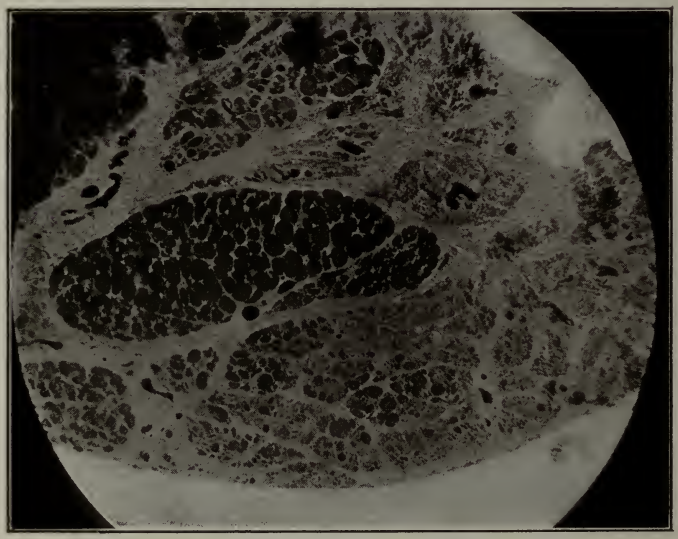


Fig. 3.—Section of a muscle from the back, showing the atrophy of many muscle fibers with a bundle of nearly normal fibers in the midst of greatly atrophied fibers.

spindles appeared to be normal. The blood-vessels within the calf muscle were much sclerosed.

A piece of the median nerve teased and stained with 1 per cent. osmic acid solution showed no pronounced degeneration by this method.

A summary of the important findings in the muscular and nervous systems in this case is as follows:

The brain was of extraordinarily large size for so young a child (25 months), and was as large as that of an adult. Excepting the large size, it presented no gross anomaly. The nerve cells of the anterior horns

in the cervical and lumbar regions were scarce, and those present were much atrophied. The anterior roots throughout the cord were considerably smaller than in a normal spinal cord, and stained imperfectly by the Weigert hematoxylin method. A peripheral nerve examined was much degenerated. The alteration of the muscles was intense, and consisted of greatly atrophied muscle fibers in the midst of other fibers well preserved, of overgrowth of sarcolemma nuclei and connective-tissue nuclei, of excess of fibrous and fatty connective tissues, of increase in size of some muscle fibers, and of fatty change within certain muscle fibers. The intramuscular nerve fibers showed degeneration. The muscle spindles appeared to be normal.

Fig. 4.—Section of muscle from the calf stained by the Marchi method, showing fatty change within a muscle fiber.

A comparison of this case and of its pathological findings with the case B. T., previously reported by one of us (Spiller), is instructive. The condition in B. T. corresponded closely with the description of the disease as given by Oppenheim. Objections have been made to it by one or two authors on two points — namely, a so-called blindness and a so-called paralysis of deglutition. Neither of these conditions was recorded in the history. The case has been accepted as typical by many, especially by such important investigators as Collier and Holmes, and Cassirer.

The baby was born at full term, and the birth was normal. It was breast-fed until the date of its admission to the hospital. Nothing abnormal in the child was noticed by the parents until he was about 5 months of age, when he did not seem to take notice of things as he should. He

had never been able to hold anything in his hands. The mother had not noticed any increase in the child's weakness since birth, and as he was very weak when he came under the observation of one of us, it is reasonable to suppose the child was equally weak at the age of 5 months. The mother was an intelligent woman, and her statements were reliable. It is presumable that so marked a weakness might readily escape detection by the parents in the first months of life, and it is equally presumable that a child so weak would not notice objects in a normal manner. So far as the ocular examination can be relied on it was negative, as shown

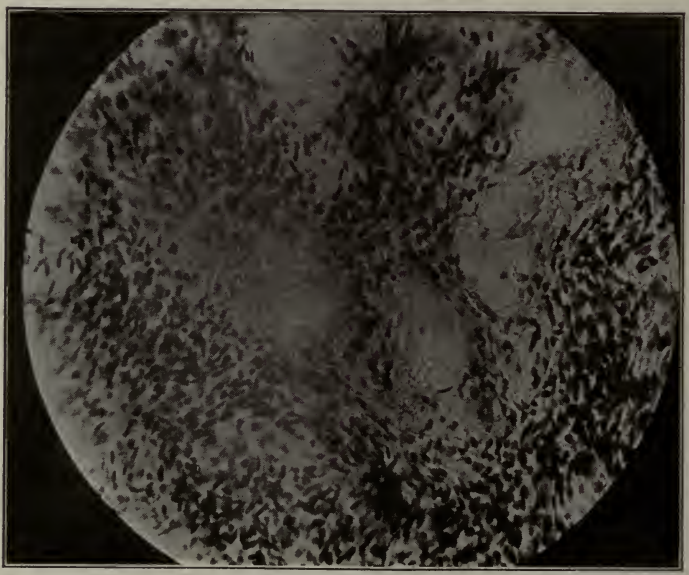


Fig. 5.—Section of muscle from the calf, showing the great excess of sarcolemma nuclei and connective-tissue nuclei and of fatty tissue.

by Dr. de Schweinitz's explanatory letter accompanying the published report.

The statement made in the report of the case might lead one to conclude that paralysis of deglutition existed, but probably such was not the case. The child was breast-fed until the time of his admission to the hospital, and had shown no difficulty in swallowing. When he was given cow's milk in an attempt to wean him he spit it out; in the report the words are, "And of late, since he has been taken from the breast, has swallowed with some difficulty."

It was not supposed that these words would be taken to mean a paralysis of deglutition. The child had swallowed well while on the breast. Inasmuch as he was 22 months of age, and possibly was not receiving sufficient nourishment, and also because it has been suggested that the development of amaurotic family idiocy may be dependent on the mother's milk (a view hardly acceptable), it seemed advisable to endeavor to have the child nourished by cow's milk. That the child would not immediately swallow this, and later swallowed it unwillingly and apparently with difficulty, in no way proves a paralysis of deglutition, and probably such paralysis did not exist. Even if it had, it would not have weakened the diagnosis in any way. As the hypoglossus nucleus has been found affected in amyotonia congenita, it is not unreasonable to suppose that the nuclei governing deglutition some day may be found implicated.

As for the objection to the case based on the existence of a squint, that has already been answered in an article published several years ago.[18] The muscular condition was typically that of amyotonia congenita, and yet the degree of weakness was not so intense as in some of the reported cases.

The pathological findings in this case are important, and the examination was complete. If more findings were not recorded, it was because they did not exist, with the exception of some alteration of the muscle from the left foot, not observed in the sections made at the time of the report. Since that time new sections have been made from all the muscles obtained, but only in those from the foot were additional findings observed. The pathological findings are recorded here in order to compare them with the findings in the case of Charles K.

"The spinal cord and brain were well developed, and the anterior and posterior spinal roots were normal. The nerve cells of the anterior horns of the cervical and lumbar regions were normal by the theonin stain. The white matter of the spinal cord was not affected, even by the Marchi stain. A nerve from the upper part of the right upper limb stained by the Weigert hematoxylin or acid fuchsin method was normal. The internal popliteal nerve and a nerve from the upper part of the right upper limb teased and stained by a 1 per cent. osmic acid solution were normal.

"Muscles from the sole of the left foot, from the back of the trunk, and from the left calf had a hyaloid appearance, and that from the sole of the foot was striking, on account of the increase in the nuclei of its

18. Spiller, Neurologisches Centralblatt, 1907, No. 11.

connective tissue. The muscle fibers were small, and those from the sole of the foot and from the left calf were much smaller than those from the back of the trunk, and the child had had more power in the muscles of the back than in those of the lower limbs. Unusually large muscle fibers were not observed. The transverse striations were well preserved, but the longitudinal were not so distinct. Nerve fibers within the muscles from the sole of the foot appeared to be normal."

It is difficult to know in what way the report of the muscular condition could have been enlarged on.

It was not asserted in the report of the case of B. T. that amyotonia congenita must be considered as a purely muscular disease. The statement was: "Congenital myatonia seems from the study of this case to be a muscular disease." It might have been well to italicize the words "this case," but it was not supposed that the statement would be taken to imply that one case could determine the pathology in all its details of a new disease.

The case of Charles K., reported in this present paper, was one of a more advanced type than that of B. T., and the findings were much more pronounced. In the former the nervous system, as well as the muscular, was greatly affected. In recently made sections from the left foot of B. T. some areas were found in which certain of the muscular fibers in bundles were more degenerated than any seen in previous sections, and these were in the midst of fibers of normal size. Some of the muscular fibers had disappeared in these areas. These findings were considerably less intense than those of the muscles in Charles K., and seem to present a transitional stage to the intense muscular degeneration of the latter case.

It is instructive to compare the findings in the reported cases. Beginning with the earliest, Spiller's case, the findings were purely muscular, and not intense although pronounced.

In Baudouin's case the changes in the nervous system appear to have been slight. In the lowest part of the eighth cervical segment the cells of the anterior horns were diminished in size and not so numerous; but one gets the impression that the diminution in number was not very great. Baudouin says: "Mais dans les groupes externes, où elles sont plus volumineuses, elles ne dépassent pas 25 microns de diamètre et sont plus rares qu'a l'état normal."

In Lereboullet and Baudouin's case the brain and cord were normal; no change in the cells of the anterior horns or in the anterior or posterior

roots was found. This case resembles that of Spiller in its findings. Some of the muscle fibers were very small, and some were very large.

In Collier and Holmes' report (case of Collier and Wilson), as well as in that of Rothmann, the changes were pronounced in the nervous system as well as in the muscles.

Reyher and Helmholz's findings were important, showing decided changes in the muscles, but no reference is made to the nervous system.

Microscopic examination of portions of muscle excised during life are reported in the cases of Bing, Collier and Holmes (first case), Openshaw, and Skoog. In the first there were practically no changes found; in the other three cases they were decided. These reports are of value as far as they go, but throw no light on the frequency of involvement of the nervous system.

A finding, so far as we know, observed only in our case (Charles K.). was the formation of fat within the muscle fibers, indicating that actual degeneration was progressing, and that the muscle change was not merely arrest of development.

From this review of the few cases as yet reported with necropsy, we may conclude that in the lighter cases (Spiller, Lereboullet and Baudouin) the alteration may be confined to the muscles, and possibly, therefore, the disease is primarily muscular, but this inference is not fully warranted. In the intense cases the nervous system is affected in marked degree. The relations to muscular dystrophy, as maintained by Batten. and to the Werdnig-Hoffmann type of muscular atrophy, as so ably set forth in Rothmann's excellent paper, are as yet undetermined. The points of resemblance to both these diseases cannot be ignored. Cassirer[17] in his recent paper has described amyotonia congenita so fully that little is left to be said on the subject. A review of the literature is given by him, as also in the early paper by one of us (Griffith[2]), and of later cases in the present contribution.

We are indebted to Dr. Allen J. Smith for the photomicrographs.

FURTHER OBSERVATIONS ON THE SOY BEAN

JOHN RUHRÄH, M.D.
BALTIMORE

In 1909, at the meeting at Lenox, I called the attention of the Society to the soy bean, and suggested its use in infant feeding.[1] Since that time I have had considerable experience with the use of the bean and also the flour made from it, and believe that it is a food of very considerable value in certain well-defined conditions, and I also believe that the bean will eventually be used as an article of diet in this country.

The composition of the soy bean I may remind you is as follows:

Water	10.13 per cent.
Protein	34.63 per cent.
Fat	17.98 per cent.
Nitrogen free extract	30.50 per cent.
Fiber	3.69 per cent.
Ash	3.07 per cent.

Calculated to a water-free basis:

Protein	38.50 per cent.
Fat	20.00 per cent.

and the analysis of the soy flour made by the Cereo Company, Tappan, N. Y., shows the following:

Protein (N. X. 6.25)	44.64 per cent.
Fat	19.43 per cent.
Mineral matter	4.20 per cent.
Moisture	5.26 per cent.
Crude fiber	2.35 per cent.
Cane sugar	9.34 per cent.
Non-nitrogenous extract	14.78 per cent.
Starch	none
Reducing sugars	none
Polarization normal weight due to optically active substance other than cane sugar (included in proteids and non-nitrogenous extract)	7.86°

1. The Soy Bean in Infant Feeding. Preliminary Report, Arch. Pediat., July, 1909.

The percentage of protein in this flour is almost one-third greater than the percentage of protein in the whole beans. This is caused by removing the coarse, fibrous hulls which contain little protein.

Each ounce of this soy flour yields about 13 grams of protein and 120 calories.

In the second communication[2] I pointed out that this soy flour used as a gruel, or the beans themselves sufficiently cooked and used as a gruel, was of value in certain cases. Still later Dr. Julius Friedenwald and myself[3] showed that the bean and the gruel were used to great advantage in cases of diabetes, both in adults and in children, although our experience with the latter is practically limited to one case. I have also another article, as yet unpublished, on the soy bean cookery, showing how the bean and the flour may be prepared as a food for human beings.

The bean has received attention from time to time in other countries, and two of the most recent contributions came from Germany and France. The first suggestion comes in the form of a patent flour made by Bayer & Company and patented in this country. This is made by treating the beans with boiling water and 0.5 per cent. of sodium bicarbonate until the carbohydrates and other water-soluble substances are removed. The residue after being dried and pulverized is a yellow powder containing the nutritive fatty and protein constituents of the beans. Goff[4] has published an article describing the soy bean and pointing out its use as a food for diabetics, and also gives a number of recipes for the preparation of various dishes made from them.

Briefly stated, the uses of the soy bean are as follows:

First, in the form of dilute gruels either with or without the addition of some starchy flour, as barley flour, in summer diarrheas and in certain forms of intestinal indigestion. These gruels are well borne in some cases where nothing else seems to agree. Later the condensed milk or cow's milk may be added to the gruel. From one to two level tablespoonfuls to the quart is usually sufficient to start with, and this may be increased to four level tablespoonfuls to the quart and, in some instances, may be made even stronger. As a general rule, this is well borne. In some instances, particularly if the soy flour is used alone or in too strong

2. The Soy Bean as an Article of Diet for Infants, Jour. Am. Med. Assn., May 21, 1910, p. 1664.

3. The Use of the Soy Bean as a Food in Diabetes, Am. Jour. Med. Sc., December, 1910.

4. Le soja dans l'alimentation des diabetiques, Gaz. d. hop., March 7, 1911, p. 399.

gruels, it may cause foul-smelling stools and evidences of intestinal putrefaction. This rarely happens if dilute gruels are used or if a certain amount of starch is added. Usually the stools are smooth and have the appearance of those of children fed on malted milk.

The second class of cases are those in which cow's milk disagrees and in which there is difficulty in finding any food containing sufficient nutriment to nourish the child. The soy bean, barley and condensed milk mixtures may be used in these cases to great advantage, and, in several instances, in which children have been fed for eight or ten months on these mixtures, the results have been surprisingly good. Orange juice or some other fresh fruit juice is advisable from time to time to prevent any tendency to scurvy.

Thirdly, in diabetes this food is of great value and serves two purposes. First, it may be prepared in a number of different ways and relieves the tedium of the ordinary diabetic diet to a very great extent, and, secondly, as Friedenwald and I have shown, the use of the bean tends to lessen the glycosuria, especially when used in connection with strict diabetic diets.

I feel that the soy bean has a very definite future assured for it, and it is chiefly for this reason that I again call your attention to it as an article of diet for infants.

Biological
Medical
rials

RJ
1
A6
v.23
Biological
& Medical
Serials

American Pediatric Society
Transactions

PLEASE DO NOT REMOVE
CARDS OR SLIPS FROM THIS POCKET

UNIVERSITY OF TORONTO LIBRARY

STORAGE